A DISSERTATION ON

HYPOTHYROIDISM AND PREGNANCY OUTCOME

Dissertation Submitted to The Tamil Nadu Dr. M.G.R. Medical University Chennai

In partial fulfillment of the regulations for the award of the degree of

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CERTIFICATE

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I hereby declare that this dissertation entitled **"HYPOTHYROIDISM AND PREGNANCY OUTCOME"** was prepared by me under the direct guidance and supervision of **Prof. DR.SEETHA PANICKER**, PSG Hospitals, Coimbatore.

The dissertation is submitted to the Dr. M.G.R. Medical University in partial fulfillment of the University regulations for the award of MD degree in Obstetrics and Gynaecology, Examination to be held in April 2013.

Place: Coimbatore **Dr. ASHMITHA THANAPPAN**

Date:

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At the outset, it is with a sense of accomplishment and deep gratitude that I dedicate this dissertation to all those who have been instrumental in its completion.

First and foremost I express my heartful thanks to my esteemed and respected HOD Department of Obstetrics and Gynaecology PSG IMSR and my guide Prof Seetha Panicker. Had it not been for her whole hearted support throughout the period of this study, extending from her vast knowledge, invaluable advice and constant motivation, I truly would not have been able to complete this dissertation topic in its present form.

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Lastly, I thank the ethics committee for permitting me to do this study and more importantly I thank all my patients involved for their kind help and co operation

LIST OF ABBREVATIONS

TSH	Thyroid Stimulating Hormone
T3	Tri iodo thyronine
T4	Tetra iodo thyronine
HCG	Human Chorionic Gonadotropin
Wks	Weeks
PIH	Pregnancy induced hypertension
IUGR	Intra uterine growth restriction
NVD	Normal vaginal delivery
LSCS	Lower segment caesarean section
PPROM	Preterm premature rupture of membranes
PROM	Premature rupture of membranes
LBW	Low birth weight
Rx	Treatment
GDM	Gestational diabetes mellitus
HTN	Hypertension

LIST OF CONTENTS

INTRODUCTION

Thyroid disorders are the second most common endocrinologic disorders in pregnancy. Hypothyroidism is mainly caused by a primary abnormality in the thyroid, although a few cases are caused by hypothalamic dysfunction also. In pregnant or postpartum women, the most common causes are chronic /subacute autoimmune thyroiditis (Hashimoto's thyroiditis)(26), iodine deficiency, radioactive iodine therapy or surgical removal of thyroid gland.

Iodine deficiency is the commonest cause. Hashimoto's thyroiditis is a common cause in industrialized nations. Overt hypothyroidism occurs in 0.3 to 0.5 % and subclinical in 2-3% of patients. Post partum thyroiditis reportedly affects 4-10% of women.

Auto immune thyroiditis occurs during the first postpartum year. They can present with hypothyroidism or thyrotoxicosis followed by hypothyroidism.

Thyroid hormone is essential for normal development of the placenta. There is evidence that preeclampsia, placental abruption and preterm labour are causally linked to faulty early placentation. Thyroid hormone is also important for neuronal migration ,synaptic transmission and myelination during early neurodevelopment. The only assumed physiological role of iodine is thyroid hormone synthesis. Severe deficiency in iodine which causes hypothyroidism is found to be associated with decreased intelligence, cretinism and even congenital anomalies of the fetus. Intra uterine growth restriction and fetal distress are more common in women with significant hypothyroidism.

These complications can be prevented if thyroxine treatment is started in 1st trimester(ideally prenatally).Treatment after 1st trimester will not eliminate already established fetal neurodevelopmental delay, because it is in the first trimester that the fetus depends completely on maternal thyroid hormone for brain development.

Thyroid function tests need to be interpreted with caution because of the changes in thyroid physiology during pregnancy. The cutoff values for diagnosing thyroid dysfunction in pregnant women is not the same as non pregnant women. The diagnosis of hypothyroidism is also difficult in pregnancy because many of the symptoms and signs are common to both. Severe hypothyroidism associated with pregnancy is uncommon because most of these women will be infertile and they also have higher rates of miscarriages.

There are not enough studies in pregnant women with hypothyroidism to see if early thyroxine supplementation and adequate treatment actually reduces the occurrence of complications. This study was undertaken to see if promptly diagnosed and adequately treated hypothyroid women were able to avert complications.

REVIEW OF LITERATURE

Historical background

Goitres (Latin- guttur), defined as enlargement of the thyroid gland have been recognised since 2700 BC. The term thyroid gland (Greek- thyreoeides, shield shaped) was however coined by Thomas Wharton in 1656.It was thought to have various functions ranging from acting as a reservoir of blood to provide continuous supply to brain to beautifying women's neck. Seaweed was considers as a treatment for goitre. In 1909, Kocher was awarded Nobel Prize for his work on the pathology, and surgery of the thyroid gland.

William Gull, Governor of Guy's Hospital, in 1874 was the first to describe myxedema and what he called a "cretinous state in the adult".In 1883, Dr. Dawtrey Drewitt presented a patient with the classical symptoms of hypothyroidism in the Clinical Society of London

The earliest oral treatment for hypothyroidism consisted of thyroid extract. The first treatment of hypothyroidism with thyroid extract in 1891, was described by George Redmayne Murray in UK. The first recorded American use was as early as 1891 by a woman who was taking it till 84 years of age.

Embryology

Around the third week of gestation the thyroid gland arises as a primitive out pouching of the primitive foregut. It originates at the base of tongue near the foramen caecum. Endodermal cells in the pharyngeal anlage thicken to form the medial

thyroid anlage. This descends in the neck anterior to the hyoid bone. During this descent the thyroid anlage remains connected to the foramen caecum by the thyroglossal duct. The thyroid follicular cells arise from the epithelial cells of the thyroid anlage. The fourth brachial pouch gives rise to the paired lateral analages which fuse with the medial thyroid anlage. The lateral analages are neuroectodermal in origin and secrete calcitonin. Colloid formation begins in the thyroid follicles by 11^{th} week of gestation.

Thyroid physiology

Iodine metabolism and increased Iodine requirement in pregnancy:

The average daily iodine requirement is 0.1mg. Fish, milk, eggs and iodised salt are rich sources of iodine. In the stomach and jejunum iodine is rapidly converted to iodide and absorbed into the blood stream. Iodide actively enters the thyroid follicular cells by an ATP dependent process. Thyroid stores nearly 90% of body's iodine. The excess plasma iodine is excreted through the kidneys.

The WHO recommends a daily intake of 250mcg of iodine for pregnant and lactating women because the increase in thyroid hormone production in pregnancy requires an equal increase in iodine availability.

D3(placental deiodinase) removes iodine from T3 & T4,generating inactive iodothyronines and reverse T3.This also prevents large amounts of T4 from crossing the placenta. Another reason for increase in iodine demand is increased GFR with an increased urinary clearance of iodine. Although the fetal thyroid starts developing by 12 wks of gestation, it cannot organify iodine till 20wks of gestation. Till that period

the maternal T4 is the only form of the hormone that can cross the placenta. Deiodinase enzyme in the fetus converts maternal fT4 to T3 in brain & other tissues. So the fetal iodine store solely demands on maternal intake during this period.

Thyroid hormone synthesis, secretion and transport:

The first step in the synthesis of thyroid hormone is iodide trapping. It is an ATP dependent active transport across the basement membrane of the thyroid follicular cells. The thyroid follicles contain thyroglobulin (Tg) which is a glycoprotein with four tyrosyl residues. The second step in the synthesis of thyroid hormones involves iodide oxidation to iodine followed by iodination of tyrosyl residues on the thyroglobulin. Both processes in this step are catalysed by thyroid peroxidase. The end products of the second step are mono and and diiodotyrosine (MIT&DIT). The third step involves their coupling to form tetraiodothyronine (T4) or one monoiodotyrosine and one diiodotyrosine molecule to form triiodothyronine (T3) or reverse triiodothyronine (rT3). Hydrolysis of the thyroglobulin molecule to release free iodothyronines (T3and T4) and mono and diiodotyrosines is the fourth step. The later are deiodinated in the fifth step yielding iodide which is reused by the thyrocyte.

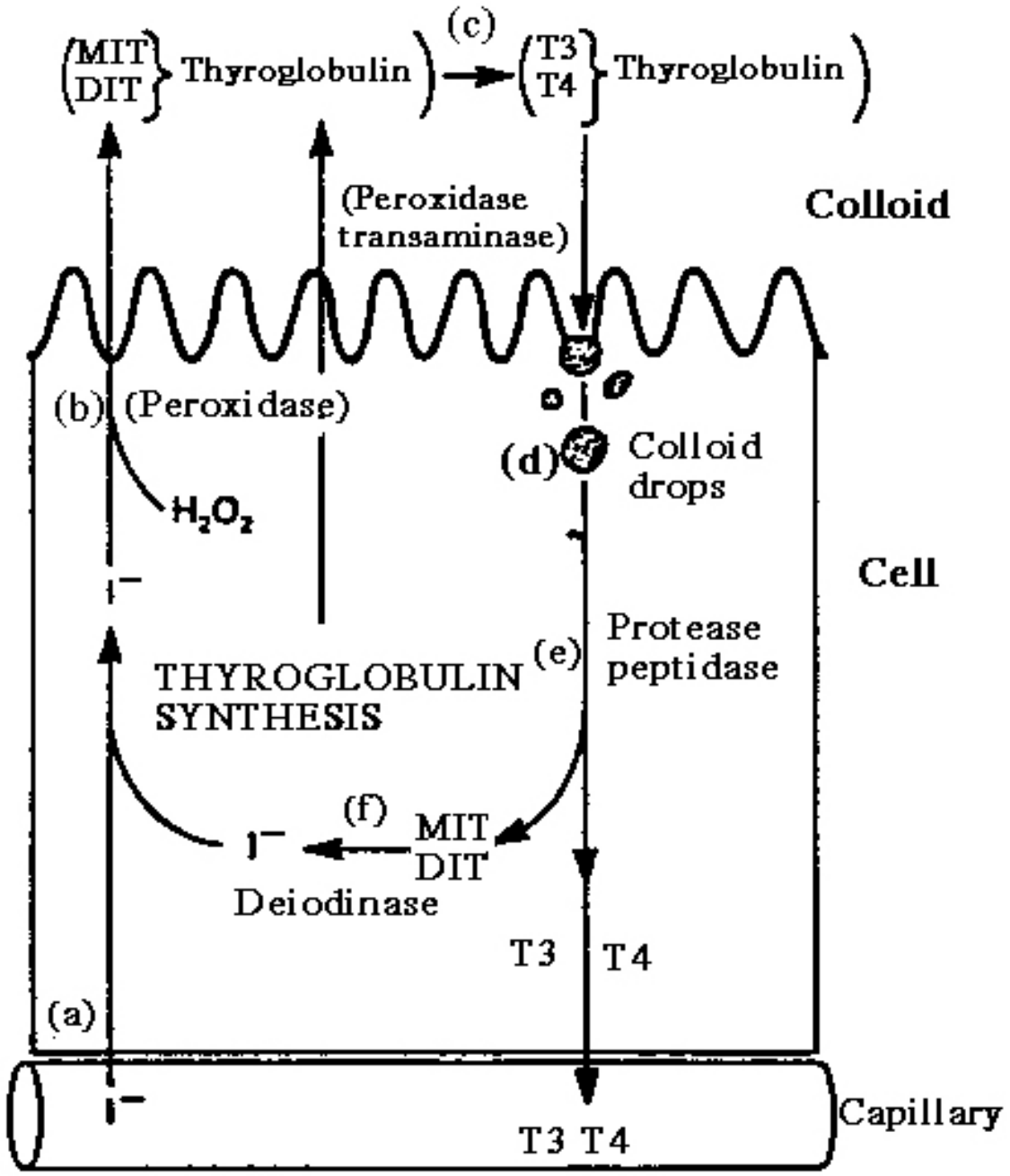


Fig : THYROID HORMONE SYNTHESIS, SECRETION AND TRANSPORT

Thyroid hormones are transported in serum bound to thyroxine binding globulin (TBG), thyroxine binding prealbumin (TPBA) and albumin. Only a small fraction of thyroid hormone is free and this is the physiologically active hormone. T3 is three to four times more potent than T4. The circulating levels of T3 are much lower when compared to T4 and is less tightly bound to proteins. Hence it enters

tissues more easily. T3 has a half life of one day while T4 has a half life of seven days.

In euthyroid state T4 is released entirely by the thyroid gland while only 20% of T3 is released by thyroid. The remaining 80% of T3 is produced by deiodination of T4 in liver, kidneys and muscles.

Metabolism and excretion of thyroid hormone:

Metabolic inactivation of T3 occurs by glucuronide conjugation and de iodination. Liver is the primary site although salaivary glands and kidneys also play a role. The conjugates are excreted in bile. A major fraction is deconjugated in the intestines and re absorbed by entero hepatic circulation to be finally excreted in urine.

Mechanism of action:

T3 penetrates cells and combines with a nuclear receptor . Certain specific DNA sequences have been identified in regulatory regions of specific genes. The T3 receptor complex binds to these specific DNA sequences leading to derepression or in some cases direct activation of gene transcription resulting in expression of predetermined pattern of protein synthesis.

Many of the clinical manifestations of thyroid hormone like tachycardia, hypertension, arrhythmias, tremor, hyperglycaemia are mediated partly if not completely by sensitisation of adrenergic receptors to catecholamines.

Functions of thyroid hormones:

Thyroid hormones enter the cells by diffusion and binding of thyroid hormones to the nuclear receptors of cells results in translation and transcription of hormone specific genes. They affect almost every system in the body.

They play an important role in fetal brain and skeletal development.

Growth and development:

Its role in growth and development can be understood by its action on the metamorphosis of tadpole to frog. Its action cannot be labelled catabolic or anabolic. It exerts a critical control over protein synthesis. Deficiency of thyroid hormone mainly affects the nervous system in early life. In cretinism there is retardation and nervous deficit as a result of paucity of synapse formation axonal and dendritic ramification and reduced myelination. In adult overt hypothyroidism also there is impairment of intelligence and movements are slow.

Intermediary metabolism:

Thyroid hormones have an important role in carbohydrate, lipid and protein metabolism.

Carbohydrate:

They stimulate carbohydrate metabolism. Although utilisation of carbohydrates is increased due to an increase in BMR, gluconeogenesis and glycogenolysis compensate for it. So hyperglycaemia and a diabetic like state occur in hyper thyroidism.

Protein:

The overall effect of T4 is catabolic. Negative nitrogen balance and tissue wasting result from prolonged action. This explains the weight loss in hyperthyroidism and weight gain in hypothyroidism. Thyroid hormones inhibit mucoprotein synthesis in low concentrations which characteristically accumulates in myxedema.

Lipid:

T4 and T3 indirectly enhance lipolysis although lipogenesis is also stimulated. Cholesterol metabolism is accelerated but its conversion to bile acids dominate. Thus hypocholesterolemia is a feature of hyperthyroidism and hypercholesterolemia and obesity are features of hypothyroidism.

Calorigenesis:

Basal metabolic rate is increased by stimulation of cellular metabolism and resetting of the energystat. But the metabolic rate in uterus, gonads, brain, spleen and lymph nodes is not significantly affected. The mechanism is uncoupling of oxidative phosphorylation thus releasing excess enegy as heat.

Cardio vascular system:

Heart rate, contractility and output are increased which cause a fast and bounding pulse. Thyroid hormones act on the contractile elements of the heart and stimulate them by upregulation of beta adrenergic receptors. They have a positive

inotropic and chronotropic effect . Actions of catecholamines are augmented. That is why fibrillation and arrhythmias are common in hyperthyroidism. It can also precipitate angina. Blood pressure particularly systolic is often raised. Myocardial oxygen consumption can be markedly reduced by induction of hypothyroidism.

Nervous system:

They maintain the normal hypoxic and hypercapnic drive in the respiratory centre of brain .Mental retardation is the hallmark of cretinism. Sluggishness and other behavioural features are seen in myxedema whereas tremors, anxiety and hyperreflexia are seen in hyperthyroidism.

Skeletal muscle:

Thyroid hormones increase the protein turnover and speed of muscle contraction and relaxation .Myxedema is characterised by flabby and weak muscles while thyrotoxicosis causes an increase in muscle tone, tremor and weakness due to myopathy.

Gastro intestinal system:

Thyroid hormones increase gastric motility. Hypothyroid patients are often constipated while diarrhoea occurs in hyperthyroidism.

Kidneys:

They have no effect in euthyroid individuals but cause diuresis when myxedematous patients are treated with them.

Haemopoiesis:

Anaemia occurs in hypothyroid individuals, thus it is proven that T4 plays a role in erythropoiesis.

Reproduction:

Oligomenorrhoea and subfertility/infertility is known to occur in women with hypothyroidism. Normal functioning of the thyroid gland is essential for maintenance of pregnancy and lactation.

Thyroid Physiology in Pregnancy:

Pregnancy is associated with changes in thyroid physiology in the mother. Thyroid hormone is derived from iodination of tyrosine residues in thyroglobulin to form mono or di iodo tyrosine which are then coupled to form T4 and T3. The majority of T4 that is released is bound to circulating transport proteins thyroxine binding pre albumin and albumin, thyroxine binding globulin (TBG). The free fraction represents 0.04% of total T4 and is the physiologically active hormone or free T4. Anterior pituitary secretes TSH which increases the synthesis and release of thyroid hormone.

During pregnancy there is an increase in estrogen mediated production of TBG.The increased binding of thyroid hormone together with its increased

metabolism by the placenta leads to a greater requirement for thyroid hormone production in order to maintain free T4 levels. Total T4 levels are above the normal non pregnant levels. There is also an increase in renal clearance of thyroid hormone in pregnancy. All these along with increase in placental transfer of iodine to the fetus in turn results in increased maternal demand for iodine which is necessary for thyroid hormone production. Women who have borderline iodine deficiency may be unable to meet this increased demand resulting in reduction in thyroid hormone production.

HCG belongs to a family of glycoprotein hormones which also includes TSH with a common alpha subunit and unique beta subunit. However there is considerable homology between beta subunits of human chorionic gonadotropin and TSH. So HCG has weak TSH like activity

Serum thyrotropin (TSH) level in early pregnancy is decreased because of thyroid stimulation from the weak TSH effects of HCG. So there is also a slight increase in free T4 levels. There are pregnancy conditions associated with higher than usual HCG levels such as a molar gestation, hyperemesis gravidarum or multiple gestation. These may result in an exaggerated stimulation of the thyroid gland and transient first-trimester thyrotoxicosis. TSH will rebound to normal nonpregnant levels once HCG returns to a steady state. So there will be a mild decline in free T4 and an increase in TSH after the first trimester. But these changes typically remain within the reference range. That is why FT4 and TSH levels should be interpreted after comparison with specific reference ranges for each trimester

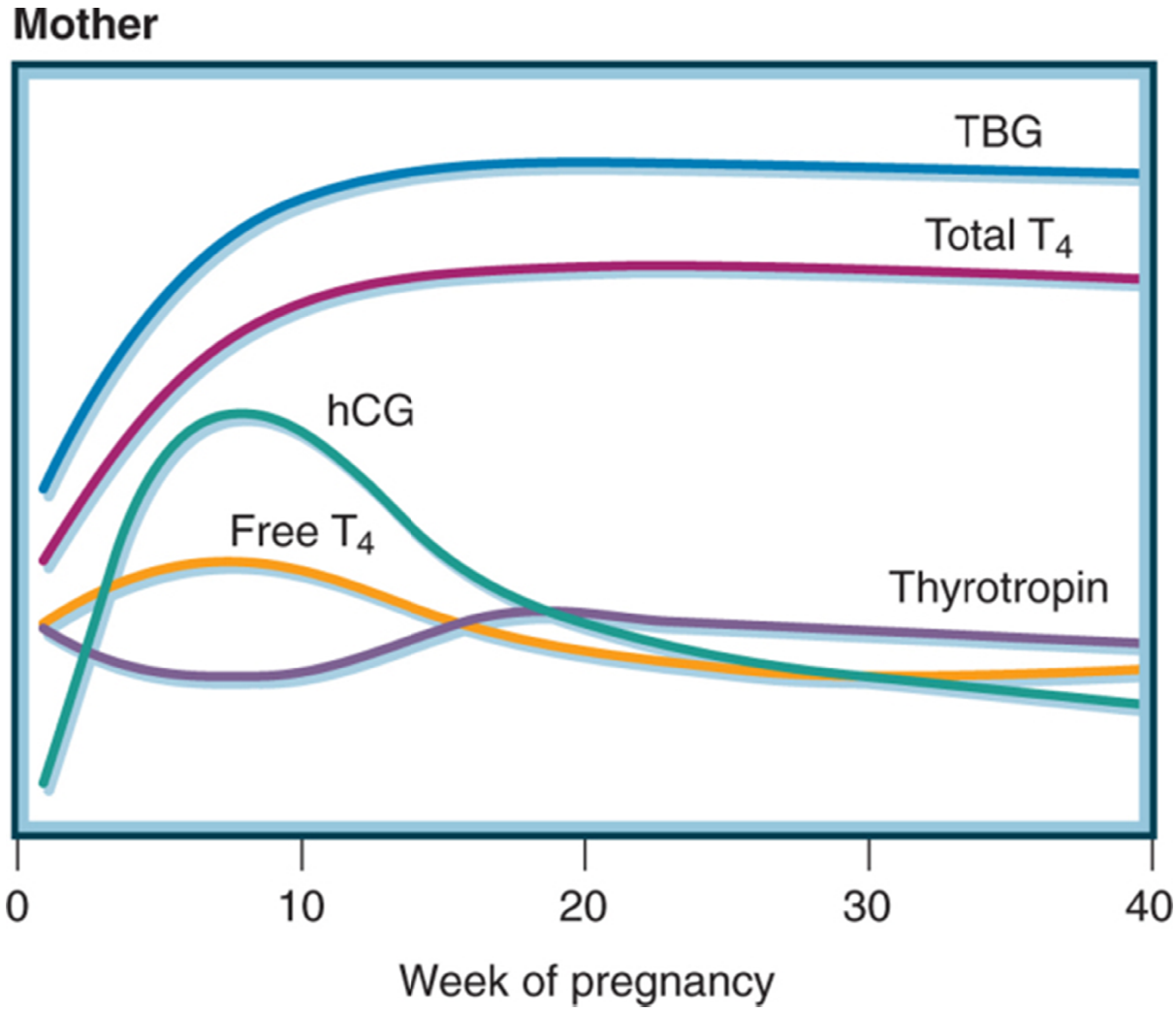
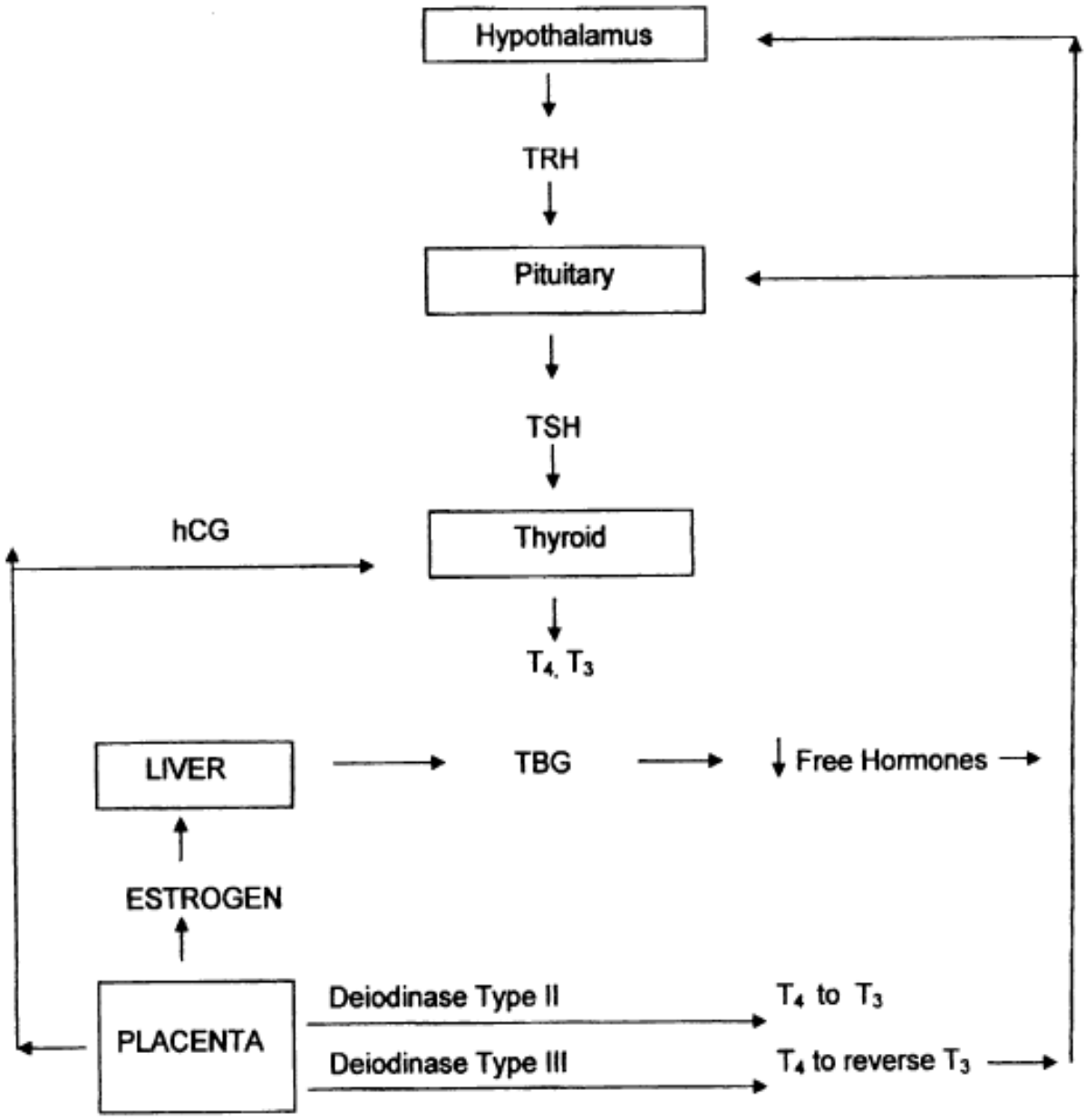


Fig: MATERNAL THYROID HORMONE LEVELS IN PREGNANCY


Hypothalamus
TRH
Pituitary
TSH
hCG
Thyroid
T4, T3
LIVER
TBG
Free Hormones
ESTROGEN
PLACENTA
Deiodinase Type II
T4 to T3
Deiodinase Type III
T4 to reverse T3

Cut off values for TSH in pregnancy:

In normal pregnancy,because of the suppressive effect of increasing thyroxin and increased TSH excretion, TSH is kept at its lowest minimal level or can even go below normal range. In populations defined as euthyroids in various studies, TSH level is always 0.1-1.6 mIU/ml and thyroxin level
is increased one and half times in pregnancy In a study by Spencer et al in 2005, S.TSH >2.5 mIU/ml in 1st trimester showed T4 insufficiency(7).

In a study by Green WL in 2005, truly normal range of TSH is defined as 0.5-2.5mIU/ml(6)

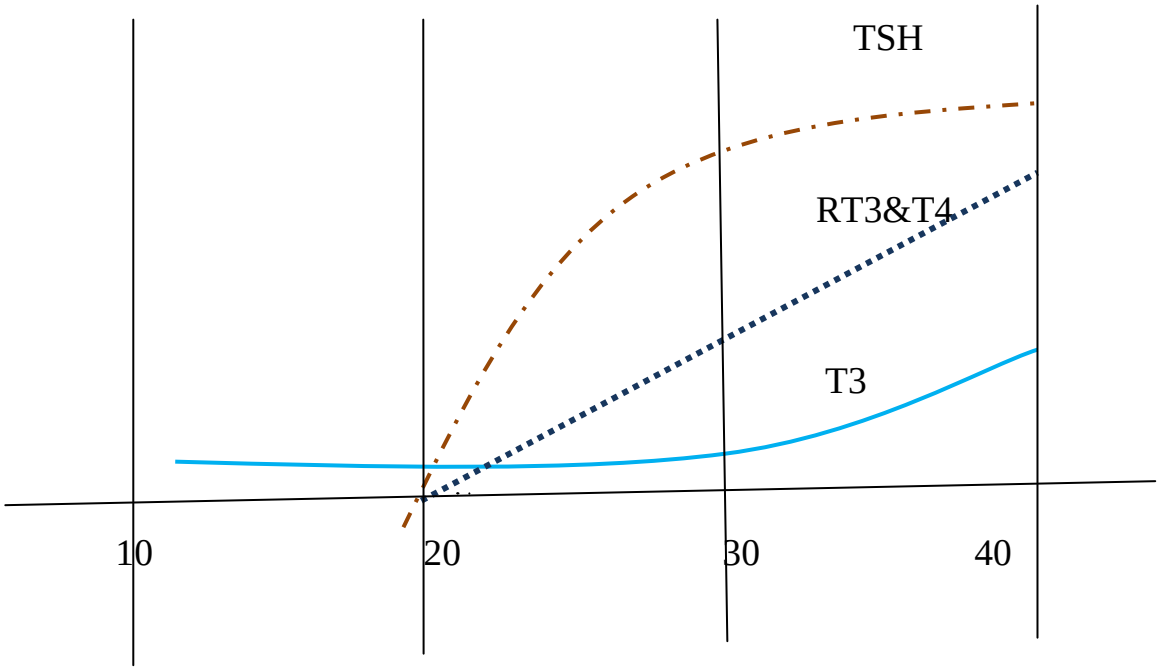
Adequate replacement therapy should be given when TSH is above 3mIU/ml and/or with low T4, FT4 in pregnancy. Prof. Ladenson has rightly said, this should be considered as Gestational hypothyroidism.

Thyroid physiology in the fetus and neonate:

The human fetus starts to concentrate iodine and to synthesise hormone between 8 and 10 weeks of gestation along with the synthesis of TSH from the pituitary. Even though the pituitary thyroid axis is completely developed at 12 to 14 weeks of gestation its function is minimal until a sudden surge in the fetal TSH occurs at 20 weeks. The fetal TSH levels continue to increase till 28 weeks after which it reaches a plateau and remains at the same level till term. Free T4

concentration increases progressively till term and exceed maternal levels. Hence some level of fetal hyperthyroidism exists at term.

Fig: FETAL THYROID PHYSIOLOGY



T4 is the major fetal thyroid hormone and the level of T3 is quite low throughout the gestation. However the levels of RT3 are elevated paralleling the rise of T4. During delivery the fetus goes from a state of relative T3 deficiency to T3 thyrotoxicosis. Shortly after birth the TSH values rise rapidly and later falls to the baseline values by 48-72 hours. In response the T4 and T3 levels increase and reach the peak values by 24-48 hours and 24 hours of age respectively. The thyroidal hyperactivity takes about 3-4 weeks to completely disappear.

The above changes occur mainly due to TRH surge as a response to rapid neonatal cooling since the TSH surge is accompanied by a prolactin surge. These thyroid changes are believed to be a protective mechanism against sudden entry of

the foetus into the cold environment. The high RT3 levels during gestation return to the baseline at 2 weeks after reaching peak levels during the first 72 hrs of life.

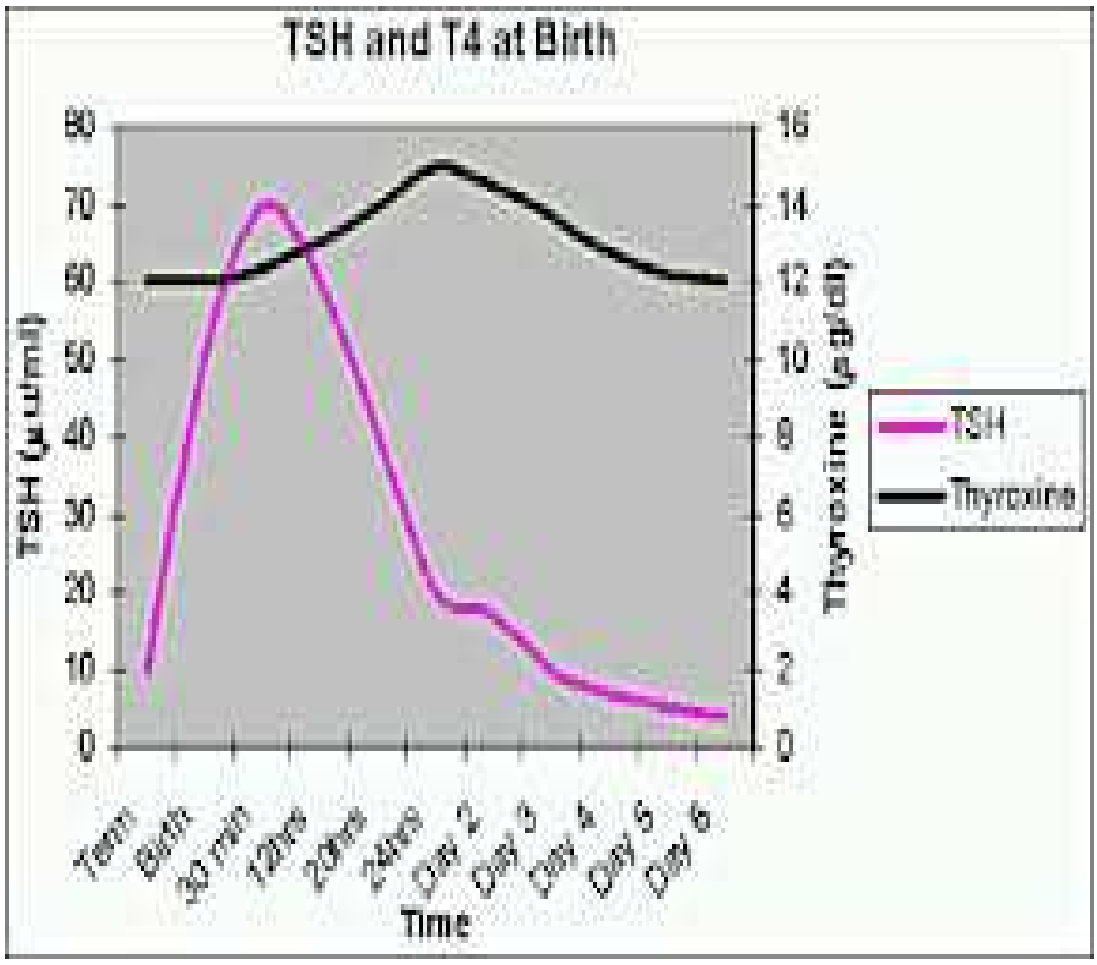


Fig: THYROID HORMONE LEVELS IN THE NEW BORN

Summary of fetal and newborn thyroid changes:

- TSH and T4 start appearing at 10-13 wks of gestation.
- Levels reach an abrupt rise at 20 wks
- T4 rapidly rises and exceeds maternal values at term
- T3T3 values rise, but levels are relatively low, similar to hypothyroid adults
- RT3 values exceed normal adult values
- The fetal pattern of low T3 and high RT3 is similar to the levels seen in calorie deprivation
- After birth, TSH peaks at 30mins, followed by a T3 peak at 24 hrs and T4 peak at 24hrs.
- High RT3 values persist for 3-5 days after birth, then plateau down to normal values by 2 wks

Maternal Hypothyroidism:

Causes of Hypothyroidism

Autoimmune	Hashimoto thyroiditis
	De Quervian's thyroiditis
Iatrogenic	Thyroidectomy
	Previous radio-iodine treatment
	Drug therapy(eg.lithium,amiodarone)
Congenital hypothyroidism	Thyroid agenesis
	Thyroid dyshormonogenesis
Iodine deficiency	(most common cause)
Infiltrative disorders	Sarcoidosis

Overt Hypothyroidism:

This is characterised by an elevated TSH and low Thyroxine levels.The incidence of overt hypothyroidism in pregnancy is 0.3-0.5%(12)

The adverse effects include miscarriages, anaemia, pre-eclampsia, abruption, PPH, premature birth, LBW, increased neonatal respiratory distress.(12)

In a study by Jones WS et al in the American Journal of Obstetrics and Gynaecology in 1969 a conclusion was made that premature deliveries were more frequent in pregnant women who had low thyroxine levels.

In a study by Leung AS et al in 1993 it was found that overt hypothyroidism resulted in an increase in incidence of gestational hypertension, preeclampsia and low birth weight babies. (14)

In a study Allan WC et al in 2000 it was concluded that fetal demises were significantly increased in patients with TSH greater than 10mIU/ml.

Davis et al 1988 followed 25 hypothyroid women through 28 pregnancies who were divided into two groups, of which 16 were clinically hypothyroid and 12 had subclinical hypothyroidism. This study showed that mothers with overt hypothyroidism are more at risk for preeclampsia, preterm delivery, placental abruption, stillbirth, postpartum haemorrhage and cardiac-dysfunction

ACOG practice bulletin on thyroid disease in pregnancy(2001) states that untreated hypothyroid patients are at a increased risk of pre eclampsia and inadequate treatment is also associated with low birth weight infants.(26)

In an Indian study by Sahu MT et al published in Archives of gynaecology and obstetrics in 2010, it was noted that IUGR ,gestational hypertension and IUD were increased in women with overt hypothyroidism.

A couple of studies have shown low thyroxine concentration in early pregnancy can be associated with low intelligent quotient of children at 7 years of age.

Ohara N et al in 2004 reviewed the literature on the role of thyroid hormone in trophoblast function and fetal neurodevelopement. They concluded that close scrutiny of maternal thyroid hormones to ensure adequate hormone levels in early pregnancy are of prime importance in preventing miscarriage and neurodevelopmental deficits in infants(15)

A study by Evelyn Man and colleagues in 1969 compared the outcomes of 1252 normothyroxinemic pregnancies with 168 hypothyroxinemic pregnancies.30 out of the 168 hypothyroid women ended up having preterm deliveries or fetal death(19.6%) compared only12.6 % in the euthyroid group.

Only few reports are available on the pregnancy outcome in hypothyroid pregnant women who are left untreated. These data show that adequate thyroxine replacement greatly improves but does not totally suppress the frequency of obstetric complications.(8)

Subclinical Hypothyroidism:

By definition,it is a condition in which TSH is elevated ,but FT4 is normal. Incidence of subclinical hypothyroidism is at least 2.5% .Usually it is asymptomatic, but there is evidence autoimmune thyroid disease (positive TPOAbs and or TG antibodies)in 50-60%(12) Subclinical hypothyroidism was found to be more common in women delivering before 32 weeks.(12)

Pregnancies complicated by subclinical hypothyroidism had a 3 fold increased risk of developing placental abruption and 2 fold increased risk of preterm labour compared to euthyroid women.(22)Gestational hypertension also occurred more commonly in these women.(23)

Even raised maternal TSH (high level of normal) is associated with neonatal respiratory distress, miscarriage and preterm delivery(12).The likelihood of patients diagnosed as hypothyroids during pregnancy to continue to be hypothyroid even after pregnancy depends on the initial TSH value.The United States Preventive Services Task force reported that nearly almost all patients with an initial TSH >10 mIU/ml developed overt hypothyroidism within 5 years.(33)

Isolated Hypothyroxinaemia:

It is defined as a condition with normal TSH and low fT4.Cleary Goldman and colleagues in 2008 screened 10,990 patients for thyroid dysfunction .They noted that

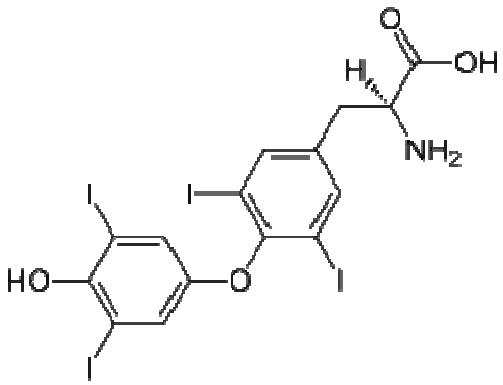
the presence of this isolated hypothyroxinemia in 1st trimester was associated with an increased occurrence of preterm delivery and and macrosomia.Its occurrence in 2nd trimester was associated with gestational diabetes.(28)

Clinical features of hypothyroidism:

Hypothyroidism developing in childhood results in delayed development and may even cause abdominal distension, umbilical hernia and rectal prolapse. Mental performance is diminished but severe retardation is uncommon. In adults mostly symptoms are non specific. They include weight gain, fatigue, intolerance to cold, constipation and menstrual irregularities like menorrhagia. Patients with myxedema have typical facial features. Skin is yellowish due to reduced conversion of carotene to vitamin A. Hair becomes brittle and there is also a characteristic loss of the outer two third of eye brow. Untreated patients can develop dementia which is called myxedema madness. There is decreased libido and fertility in both sexes. Cardio vascular changes include bradycardia, pericardial or pulmonary effusions.

Treatment of Hypothyroidism:

Levothyroxine



Levothyroxine or T_4, is a synthetic form of the thyroid hormone , which is normally secreted by the thyroid follicular cells . Levothyroxine is chemically in the chiral L-form. Edward Calvin Kendall of the Mayo clinic first isolated thyroxine in its pure form from extracts of hog thyroid glands in 1914. The hormone was synthesised by British chemist Charles Robert Harington in 1927.

Absorption of L thyroxine is incomplete varying from 50-70%. For most therapeutic purposes L thyroxine is superior to lio thyronine because of its longer duration of action. The only accepted indication for the use of lio thyronine is myxedema coma where a quick response is essential.

Levothyroxine should be taken on an empty stomach approximately half an hour before meals.

Patients should avoid taking calcium and iron supplements within 4 hours of taking thyroxine as these can interfere with the absorption of this drug.

According to the American Thyroid Association,pregnant women already being treated with thyroxine hormone often require a 30-50% increase in dose.The

need for the increase in dose starts as early as 5 weeks of gestation. The association urges physicians to be vigilant in identifying and treating women with subclinical thyroid dysfunction before conception.

The Journal of Clinical Endocrinology and Metabolism published an Executive Summary which stated that,in patients with overt hypothyroidism the dose of thyroxine should be adjusted to reach a TSH not more than 2.8 IU/ml periconceptionally. The Thyroxine dosage usually needs to be increased by 4-6 wks of gestational age and may require a 30-50% increase. If a patient is diagnosed to have overt hypothyroidism during pregnancy, titrate the dose rapidly to keep the TSH at a level less than 2.5 IU/ml in the first trimester and less than 3 IU/ml in second and third trimesters. The panel recommends also thyroxine replacement in women with subclinical hypothyroidism.

Complications of hypothyroidism in pregnancy:

- Spontaneous abortion
- Pregnancy induced hypertension(pre eclampsia, eclampsia)
- Placental abruption
- IUGR
- Oligohydramnios

- Preterm delivery
- Fetal distress
- Low birth weight

Congenital Hypothyroidism:

Congenital Hypothyroidism (CH) is one of the most common preventable causes of mental retardation. The incidence is 1:4000 livebirths and the worldwide and the incidence in India is 1:2500-2800 live births.

Thyroid dysgenesis is the commonest cause attributing for the majority of cases. CH can be permanent or transient. Maternal cytotoxic antibodies and genetic

mutations causing inactivation of thyroid receptor can be a cause.There is clinical and scientific evidence that hypothyroxinemia causes poor neurodevelopment outcome in the children of mothers with low thyroxine levels.

In a study by Morreale de Escobar et al in2004,it was noted that thyroid hormone accumulates in the cerebral cortex before 20 weeks.(30)

Primary evidence of the effect of the deficiency of thyroid hormone on cerebral cortex was studied by Lavado-Autric et al in 2003.(31)

Defects in thyroid hormone synthesis account for 10% of all cases. These can be inherited as autosomal recessive disorders. Pharoah et al did a landmark study in 1971 and came to a conclusion that iodine supplementation in pregnancy prevented subsequent cretinism.

Early and aggressive treatment with thyroxine is crucial for infants with congenital hypothyroidism. Yet some infants with prompt replacement exhibit mild cognitive defects in adolescence.(47)

CLINICAL FEATURES OF CONGENITAL HYPOTHYROIDISM

Untreated severe congenital hypothyroidism leads to irreversible growth failure and mental retardation

- Early symptoms include feeding problems, constipation, growth failure and hoarse cry

- Later they develop dry skin and decreased growth of nails and hair; tooth eruption is delayed
- Closure of anterior and posterior fontanellesis delayed
- Cardiomegaly may be present

The other clinical features are broad, flat nose, pseudohypertelorism, puffy, myxedematous facies, large, protruding tongue, prolonged neonatal jaundice, protuberant abdomen, umbilical hernia

Postpartum Thyroiditis:

Postpartum thyroiditis is a characterized by a lymphocytic infiltration of the thyroid gland .It's reported incidence is in about 5% of pregnancies(17).It usually occurs in the 1st month after delivery.It starts as a thyrotoxic phase followed by a phase of hypothyroidism lasting for months.It is typically characterized by the presence of TPO antibodies although it's occurrence is women without these antibodies has also been reported.The risk is even greater when TPO antibodies are detected antenatally.Studies have shown that as many as 50% of women who developed postpartum thyroiditis continued to remain hypothyroid at the end of the 1st postpartum year. There is no compelling evidence to support the early treatment of this condition.

Thyroid antibodies:

- These tests do not determine the thyroid function, instead they indicate the underlying disorder. Antithyroglobulin, antimicrosomal and thyroid stimulating immunoglobulin are the thyroid antibodies. Approximately 80% of patients with Hashimoto's thyroiditis have raised thyroid antibody levels.

- Thyroid peroxidase(TPO)antibodies and AntiThyroglobulin(TG) antibodies are linked to pregnancy complications. There are studies to show that euthyroid women with recurrent miscarriages and preterm birth were found to have antibodies to either TPO or TG.TPO antibodies have also been implicated in the development of postpartum thyroiditis.

- Association between auto immune thyroiditis and adverse obstetric outcome independent of thyroid function has also been proven in another prospective study where euthyroid TPO antibody positive women who received thyroxine supplementation in early pregnancy had a reduced rate of miscarriage and preterm delivery rate(12)

- Pregnant women with TPO antibodies were found to have a three times more chances of placental abruption when compared with antibody negative controls in a study by Abbassi-Ghanavati et al in 2010.

- Pop et al revealed decrease in the intelligent quotient of children aged 5 years whose mothers were TPO antibody positive at 32 weeks of gestation even though they were actually euthyroid.(4)

- Some thyroid autoantibodies cross the placenta causing fetal thyroid dysfunction. But maternal Hashimoto thyroiditis is not typically found to be associated with fetal thyroid abnormalities.

- Brown and co-workers in 1996 did a study on over one million babies and found that only 1 in 180,000 neonates born to mothers with Hashimotos thyroiditis had thyroid dysfunction.(46)

Hypothyroidism and Infertility:

Infertility is defined as the inability to conceive after one year of intercourse without contraception (39)

In mild degrees of hypothyroidism, ovulation and conception can occur, but the pregnancies that result are complicated by abortions, stillbirth or prematurity (13).On the other hand, severe hypothyroidism is commonly associated with ovulatory dysfunction and, thus, infertility. Hypothyroid women can present with menstrual irregularities, especially oligomenorrhoea.

Thyroid underfunction can also act more indirectly, by altering the HPO axis, by reducing the binding activity of sex hormome-binding globulin (SHBG)causing an increase in serum free testosterone and estradiol, by decreasing the metabolic clearance of androstenedione and estrone. Also, TRH is elevated in hypothyroidism which causes an increase in prolactin levels, and a delay in LH release to LH-releasing hormone (LHRH). Treatment of thyroid underfunction with L-thyroxine (L-T4) usually restores a normal menstrual pattern and alleviates these pathological mechanisms (34)

It has been recently recognised that disturbances of cognition and mood develop in association with alteration in thyroid metabolism in the brain. There are even few small studies to show the connection between thyroid dysfunction and mood disorders like postpartum depression .

Thyroid Dysfunction and pregnancy loss:

Normal thyroid function is critical for normal functioning of the gonadal axis, thus important in maintaining normal reproduction.

Gonadal steroid synthesis by oocytes depends on an adequate level of thyroid hormones. T3 modulates the regulating action of LH and FSH on steroid biosynthesis, thyroid hormones increase and enhance estrogenic responses(9). Dysthyroidism is associated with anovulatory cycles, subfertility or infertility

Abortion rate as high as 60% in inadequately treated overt hypothyroids and 70% in subclinical hypothyroids(10)

Matsua et al showed that Free T_3 and Free T_4 values were significantly lower in women whose pregnancies terminated in abortions .(40)

Donmez M et al in 2005 did a case control study to investigate thyroid dysfunction as an causative factor for abortions. They performed thyroid function tests in 60 patients having spontaneous miscarriages and compared them with those of 40 pregnant women of same gestational age who were presumed to reach term. They found that T_3 and T_4 values were significantly lower and TSH values were significantly higher among the abortion group suggesting that subclinical hypothyroidism may be responsible for the spontaneous abortions[(16)]

There are theories that consider autoimmune thyroiditis a consequence of increased lymphocytes T activation. Patients with antecedents of habitual abortions

show an increased number of endometrial T lymphocytes. Expression of the antithyroid antibodies may be an epiphenomenon that reflects an autoimmune imbalance, causing the rejection of the product of conception. This hypothesis is supported by the existence of an increased CD5/20 lymphocyte positivity in women with recurrent miscarriage(11)

In 1990 Stagnaro- Green et al showed that among 552 women who were screened for thyroid antibodies , abortion rate of 17% was observed in antibody positive group as compared to 8.4% in anti body negative group.(18)

Bussen Steck et al in 1995 screened 22 non pregnant women with bad obstretic history for thyroid antibodies and detected a higher prevalence of thyroid antibodies in 36% compared to 9% in multiparous controls and 5% in nulliparous controls.(19)

Matalon ST et al in 2001showed that elevated levels of thyroid autoantibodies are associated with increased rate of abortions in euthyroid women.(20)

Vaquero et al in 2000 studied pregnancy outcomes in patients with mild thyroid abnormalities. Women mild thyroid abnormalities had an increased rate of miscarriage. Thyroid replacement therapy with intra-venous immunoglobulins (IVIG) was helpful in preventing a new miscarriage (37)

A study by Pratt et al found that the incidence of anti-thyroid antibodies in women who had repeated abortions were noticeably higher than other non-organ-specific auto-antibodies(38)

Screening for thyroid dysfunction during pregnancy:

For universal screening to be recommended for a disease,

- The incidence of the disease should be high enough to warrant screening.
- The screening needs to be as cost effective as possible
- There should be substantiative evidence that adverse outcomes are associated with the disease.
- There should also be evidence that intervention improves outcomes.

The journal of clinical endocrinology and metabolism adopted a clinical practise guideline in 2007 which recommended screening among the following high risk women(27)

a) Women with a previous history of hyper /hypo thyroid disease / thyroid ectomy/goitre
b) Women with family history of thyroid dysfunction
c) Women with symptoms/signs suggestive of thyroid dysfunction
d) Women with autoimmune diseases like Type 1 DM
e) Women with a history of infertility
f) Women with history of head and neck irradiation
g) Women with history of recurrent miscarriages or preterm deliveries .

According to the ACOG Committee Opinion no.381(oct 2007) also thyroid screening in pregnancy should be carried out only on symptomatic women / those with a history of thyroid disease or other medical illnesses that may be associated with thyroid disease (eg:diabetes)

In a study by Bijay Vaidya et al published in JCEM in 2007,they found that thyroid function testing of only high risk women would miss about $1/3^{rd}$ of women with overt/subclinical hypothyroidism.(21)

AIMS OF THE STUDY

Primary Aim:

To assess the benefits and pregnancy outcome in promptly diagnosed and adequately treated antenatal hypothyroid women.

Secondary Aims:

To assess whether unfavourable pregnancy outcome and complications are more among the antenatal women who are diagnosed late in pregnancy and hence inadequately treated.

MATERIALS AND METHODS

To measure pregnancy outcomes in all the study subjects, all antenatal women in their first trimester (first booking) or if they have their first visit only in second trimester will be screened with serum TSH. If TSH is more than 3miu/ml, they will be started on treatment after doing an FT4.They will be monitored to see if their treatment is adequate by repeating a serum TSH again in 2^{nd} and 3^{rd} trimesters. These women will be followed up till term and watched for any complications. Finally, they will be analysed to see if there is a significant increase in complications in the antenatal women who were diagnosed and started on treatment late and whether these complications could have been avoided if they were to be started on treatment early in the course of pregnancy

Inclusion Criteria:

a) All first and second trimester antenatal women with singleton gestation which will include overt hypothyroid women who are already on treatment(who have been informed about the study and who are willing to pay for the blood test)

b) Women with subclinical hypothyroidism (elevatedTSH, normal fT4)

Exclusion Criteria:

Multiple gestation

ESTIMATION OF FREE T_3

Method

RIA (Radio Immuno Assay) – IMMUNOTECH Prague, Czech republic

Principle

The radio immuno assay of the free tri-iodo thyronine (T_3) is a competitive assay done by using labeled antibody. Samples and calibrators are incubated with an ^{125}I- labelled antibody specific for T_3, as tracer, in tubes coated with an analog of T_3 (ligand). The free tri-iodo thyronine and the ligand compete for the binding to the labeled antibody. The content in the tubes is aspirated after incubation and bound radioactivity is measured. A calibration curve is designed and values are ascertained by interpolation from the curve.

Reagents

- ✓ Ligand-coated tubes
- ✓ ^{125}I- labeled monoclonal antibody
- ✓ Calibrators
- ✓ Control serum

Specimen collection

Blood was collected in dry tubes or in tubes containing EDTA, in a fasting state. Serum/Plasma was separated from cells by centrifugation. Samples were stored at 2-8^{0}C.

Results

Normal range of Free T_3 was taken as 2.5 – 5.8 pM/L.

ESTIMATION OF FREE T_4

Method

RIA (Radio Immuno Assay)

Principle, Reagents and procedure are similar to Free T_3 estimation.

Results

Normal range of Free T_4 was taken as 11.5 – 23 pM/L.

ESTIMATION OF TSH

Method

Solid Phase Two-Site ImmunoRadoMetric Assay (IRMA) with IRMAK-9 kit, BRIT, Mumbai.

Principle

In IRMA, two antibodies generated against different portions (epitopes) of the same antigen are used. One of the antibodies is bound to a solid phase, while the other is labeled with ^{125}I. Thus, the antigen binds both antibodies in a "sandwich" fashion. The radioactivity in the bound fraction is quantitated using a gamma counter.

Reagents

- ✓ hTSH monoclonal antibody coated tubes
- ✓ ^{125}I- Anti hTSH
- ✓ Wash diluents
- ✓ Control

Specimen collection

Serum or plasma can be used for assay.

EDTA plasma is not used.

Results

Normal range of TSH was taken as 0.17 – 3 µU/ml.

Statistical Method:

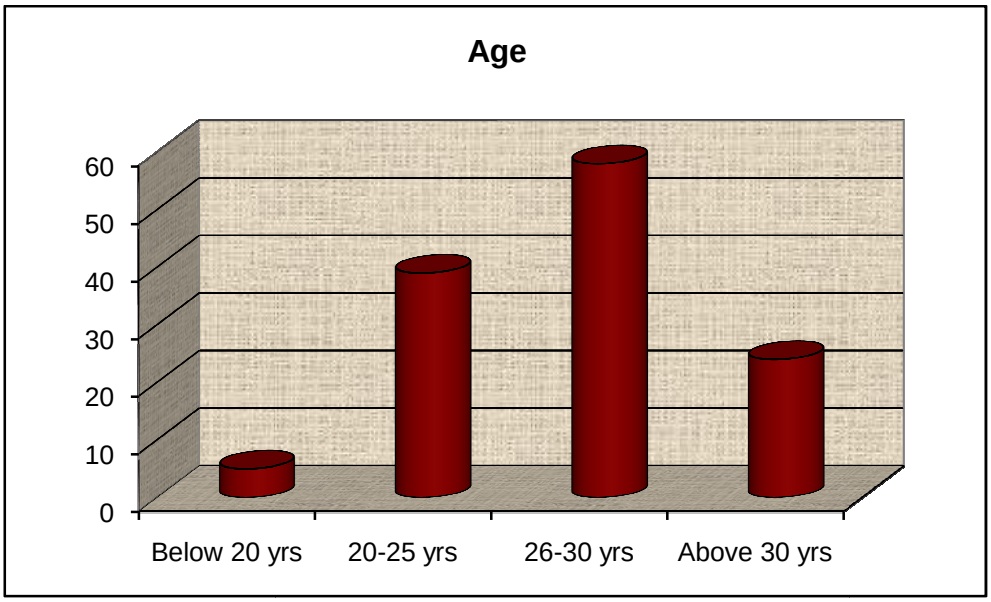
The statistical package which was used for doing the analysis was SPSS 16.00 version . Raw data were analysed using cross tabulations and Chi square test

OBSERVATION

TABLE – I

AGE DISTRIBUTION

	Frequency	Percent
Less than 20 yrs	5	4.0
20 - 25 yrs	39	31.0
26 - 30 yrs	58	46.0
More than 30 yrs	24	19.0
Total	126	100.0



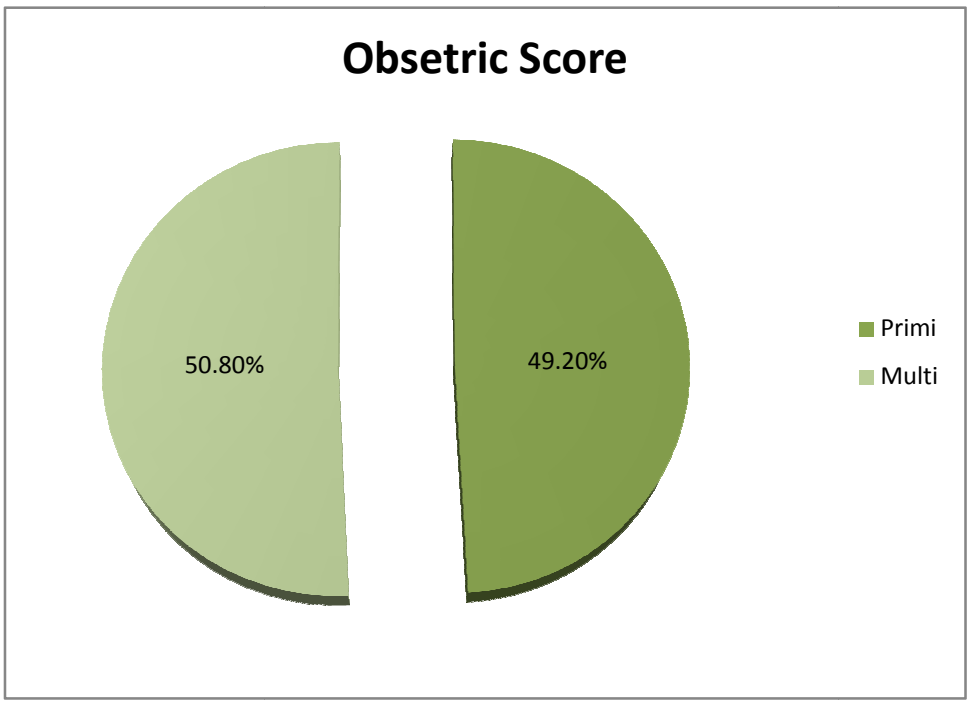


TABLE - II

Obstetric Score

	Frequency	Percent
Primi	62	49.2
Multi	64	50.8
Total	126	100.0

TABLE - III

GESTATIONAL AGE AT DIAGNOSIS

	Frequency	Percent
Preconceptional	36	28.6
Less than 10 weeks	45	35.7
More than 10 weeks	45	35.7
Total	126	100.0

This table shows the gestational age at which hypothyroidism was diagnosed

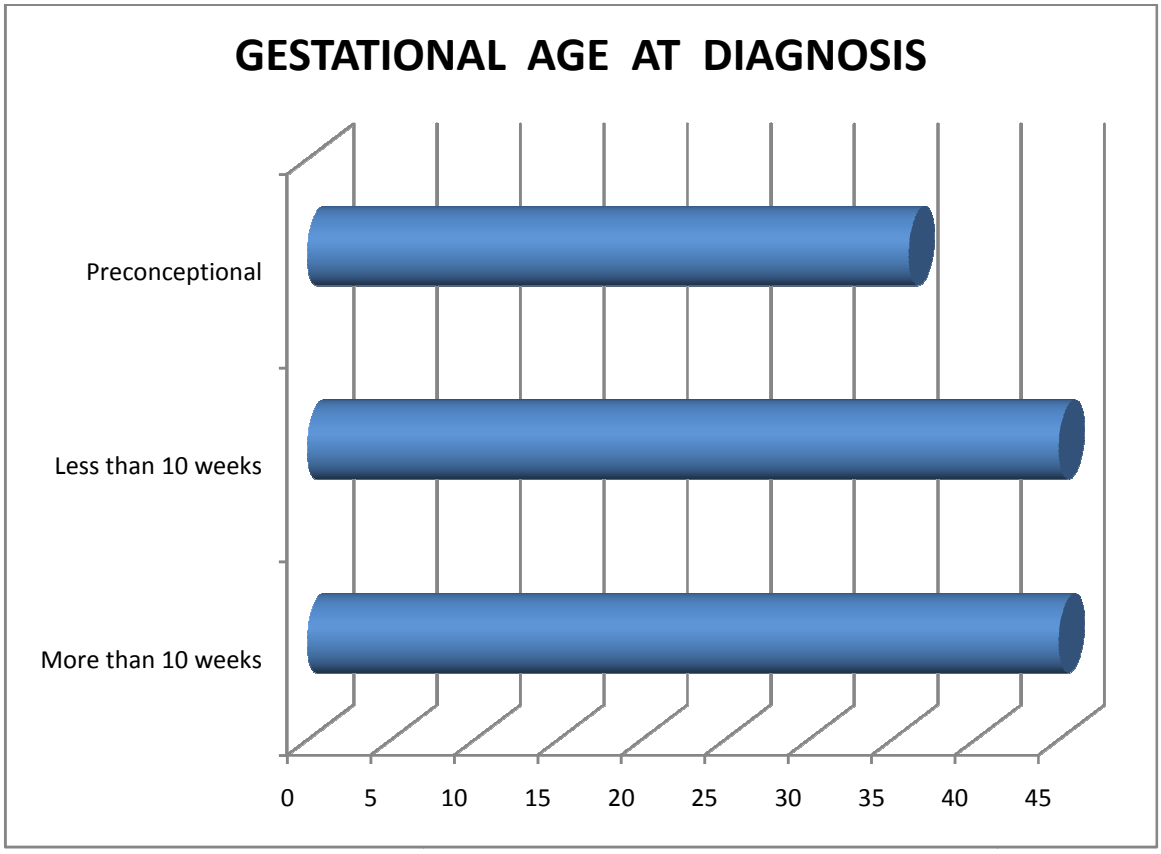
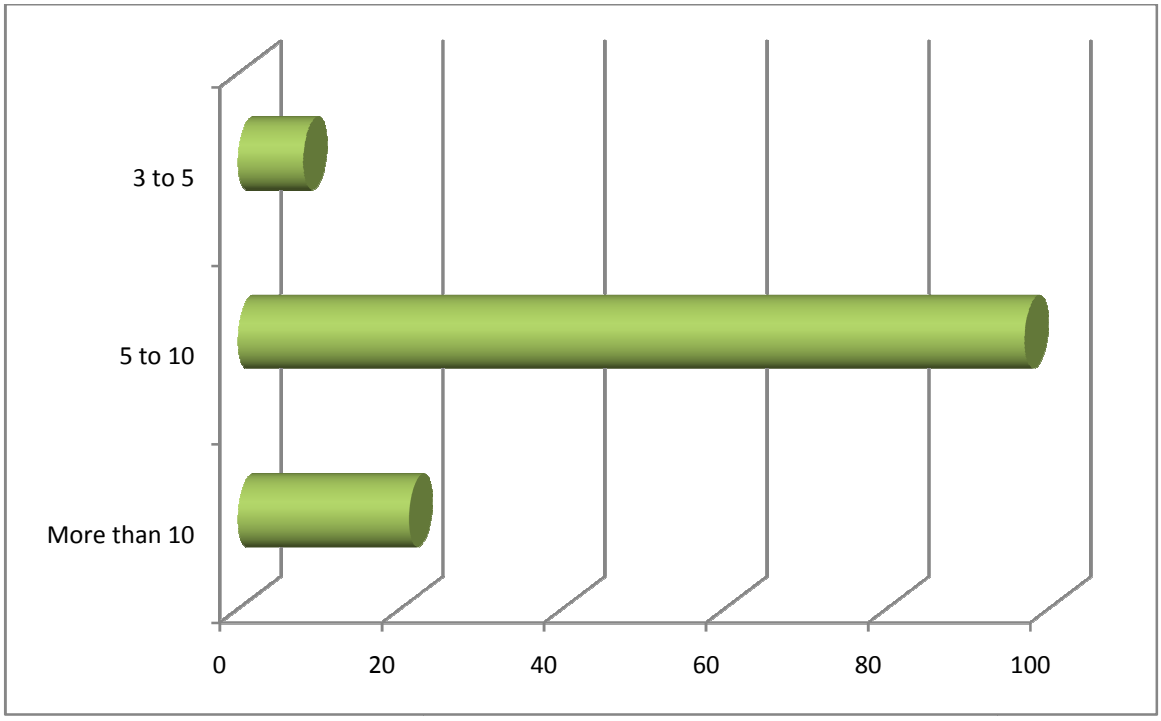


TABLE- IV

TSH AT DIAGNOSIS

	Frequency	Percent
3 to 5	8	6.3
5 to 10	97	77.0
More than 10	21	16.7
Total	126	100.0

This table shows the levels of TSH in mIU/ml at the time of diagnosis. Most of the diagnosed hypothyroid patients had TSH levels between 5 and 10mIU/ml



TSH AT DIAGNOSIS

TABLE -V

ADEQUATE OR INADEQUATE TREATMENT

	Frequency	Percent
Adequate treatment	59	46.8
Inadequate treatment	67	53.2
Total	126	100.0

This table shows that out of the 126 patients in our study group 59 received adequate treatment and 67 received inadequate treatment.

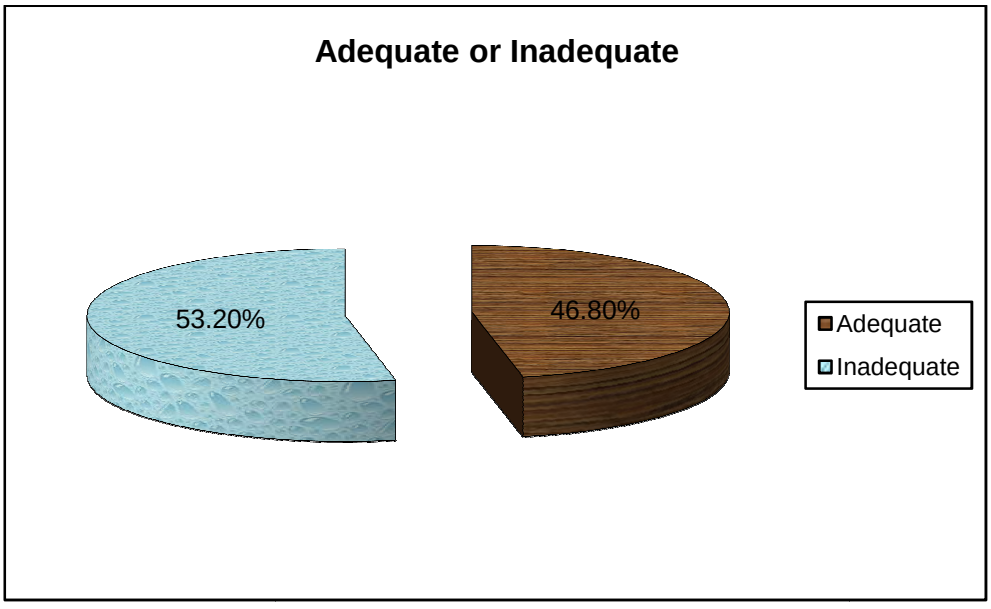


TABLE – VI

NUMBER OF PATIENTS WITH COMPLICATIONS

	Frequency	Percent
Yes	50	39.7
No	76	60.3
Total	126	100.0

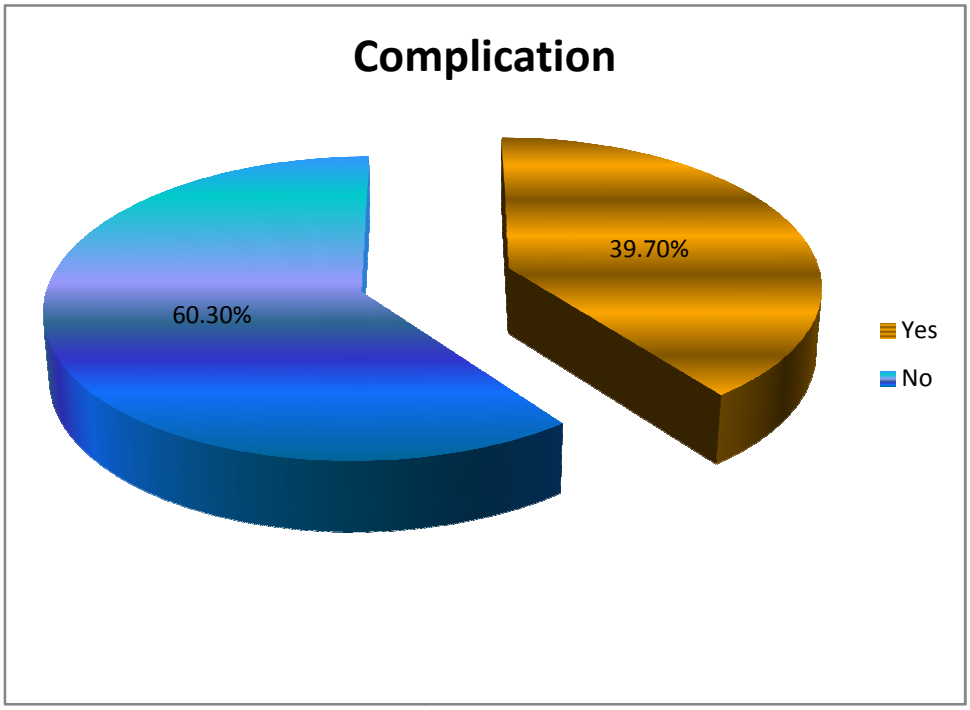


TABLE – VII

LIST OF COMPLICATIONS

2nd trimester abortion	1
Blighted ovum	1
Chronic HTN	1
PIH	11
Incomplete abortion	2
IUGR	5
Missed Abortion	3
No	78
oligohydramnios	8
Preterm delivery	15

This table shows the profile of complications encountered in our patients

TABLE - VIII

MODE OF DELIVERY

	Frequency	Percent
Elective LSCS	15	12.60
Emergency LSCS	32	26.89
Forceps delivery	1	0.84
NVD	42	35.29
Preterm delivery	15	12.60
Vacuum	14	11.78
Total	119	100.00

This table shows the modes of delivery of patients in our study group. Out of the 126 patients 7 had first trimester abortions and the modes of delivery of the remaining 119 patients are enlisted here.

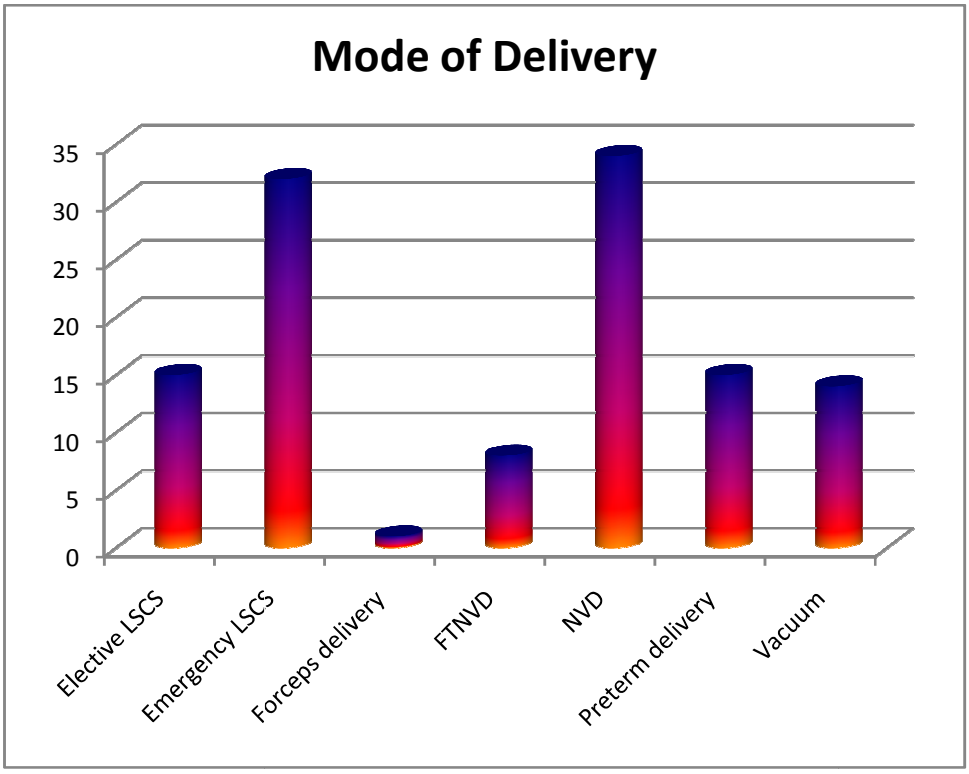

Mode of Delivery
35
30
25
20
15
10
5
0
Elective LSCS
Emergency LSCS
Forceps delivery
FTNVD
NVD
Preterm delivery
Vacuum

TABLE- IX

GESTATIONAL AGE AT DELIVERY

	Frequency	Percent
Less than 37 wks	15	12.6
More than 37 wks	104	87.3
Total	119	100

This table shows that 15 out of the 126 patients had a preterm delivery before 37 weeks of gestation.

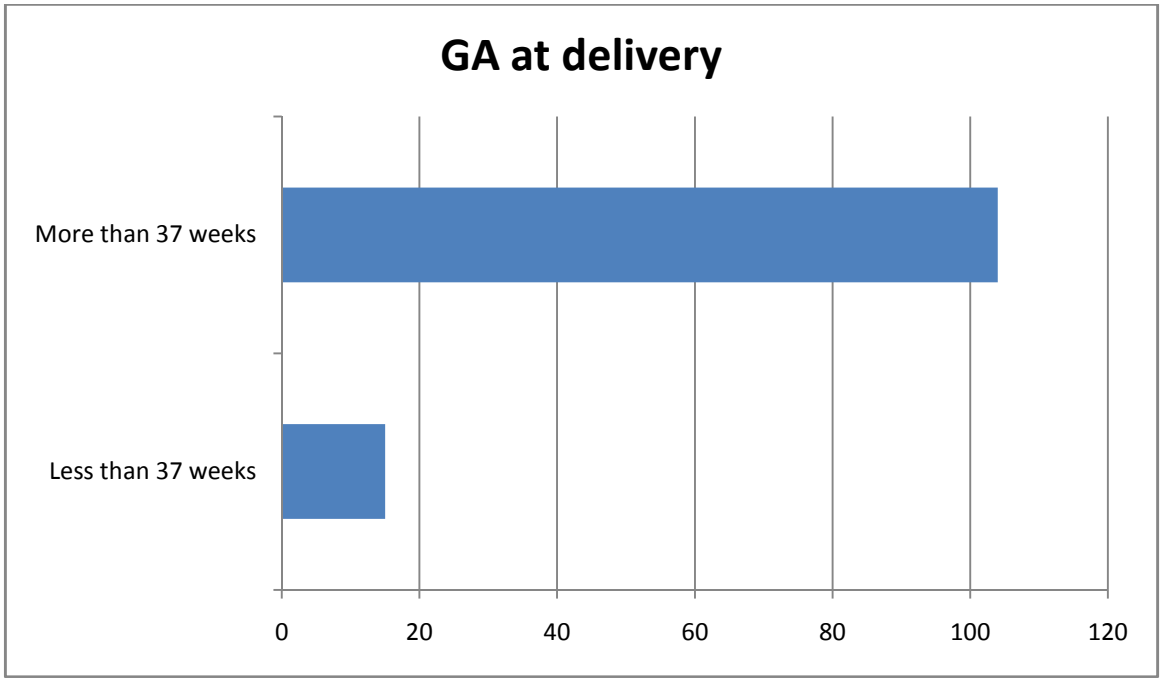


TABLE - X

Crosstabulation between complication in the adequate and inadequate treatment groups

			Complication		Total
			Yes	No	
	Adequate Rx		7	52	59
		%	11.9%	88.1%	100.0%
	Inadequate Rx		43	24	67
		%	64.2%	35.8%	100.0%
Total		Number	50	76	126
		%	39.7%	60.3%	100.0%

Chi square value 35.872.p value<0.01

Significance value 0.000

This table shows that 64.2% of the inadequately treated patients developed complications while only 11.9% of the adequately treated group developed complication which was statistically significant,

TABLE - XI

PREVALANCE OF GESTATIONAL DIABETES IN HYPOTHYROID PATIENTS

	Frequency	Percent
GDM on diet	7	58.33
GDM on insulin	5	41.66
Total	12	100.0

In my study 12 out of the 126 hypothyroid patients also had gestational diabetes mellitus , prevalence rate of 9.5%

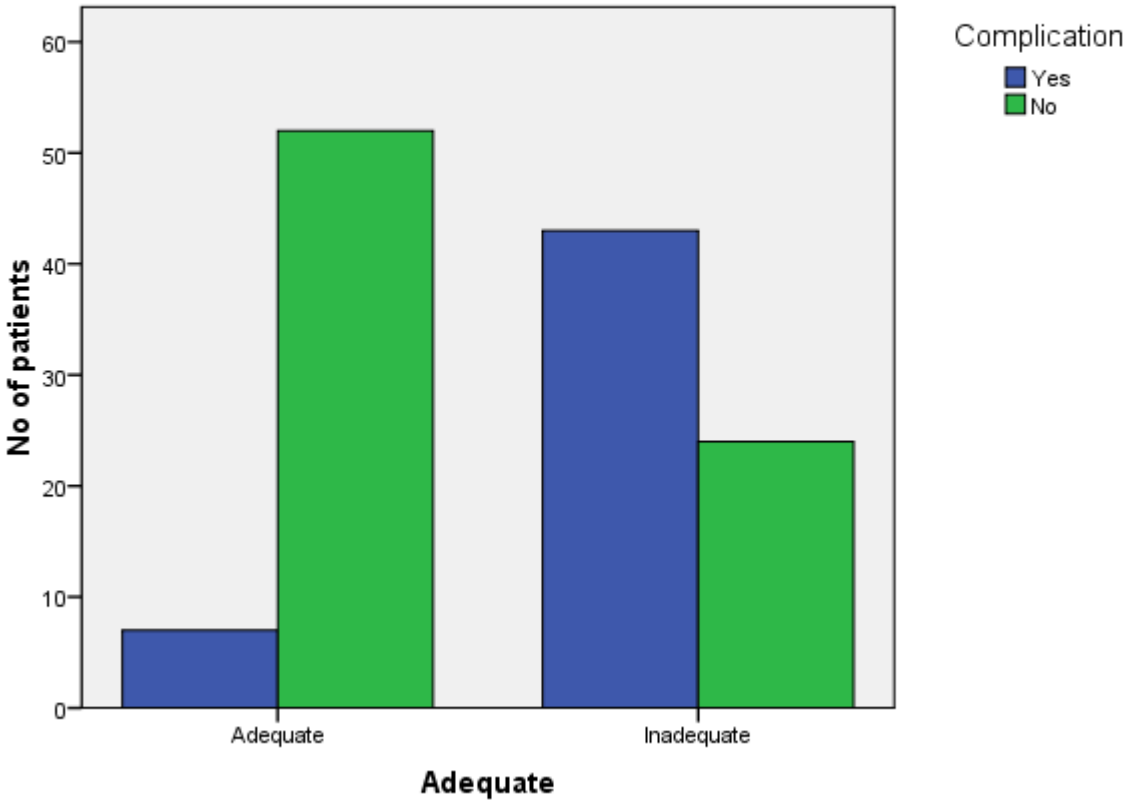

Complication
Yes
No
No of patients
60
50
40
30
20
10
0
Adequate
Inadequate
Adequate

TABLE - XII

Complication		Adequate		Total
		Adequate	Inadequate	
2nd trimester abortion	No	1	0	1
	%	1.7%	.0%	.8%
Blighted ovum	No	0	1	1
	%	.0%	1.5%	.8%
Chronic HTN	No	1	0	1
	%	1.7%	.0%	.8%
PIH	No	1	10	11
	%	1.6%	14.9%	8.7%
Incomplete abortion	No	0	2	2
	%	.0%	3.0%	1.6%
IUGR	No	0	5	5
	%	.0%	7.4%	4.0%
Missed Abortion	No	0	3	3
	%	.0%	4.5%	2.4%
No	No	52	26	78
	%	88.1%	38.8%	61.9%
oligohydramnios	No	2	6	8
	%	3.4%	9.0%	6.3%

Preterm delivery	No	2	13	15
	%	3.4%	17.9%	11.1%
Total	No	59	67	126
	%	100.0%	100.0%	100.0%

TABLE XII

PREVALANCE OF LOW BIRTH WEIGHT IN THE STUDY GROUP

			Low Birth weight		Total
			Yes	No	
Adequate	Adequate	No	8	51	59
		%	13.6%	86.4%	100.0%
	Inadequate	No	15	52	67
		%	22.4%	77.6%	100.0%
Total		No	23	103	126
		%	18.3%	81.7%	100.0%

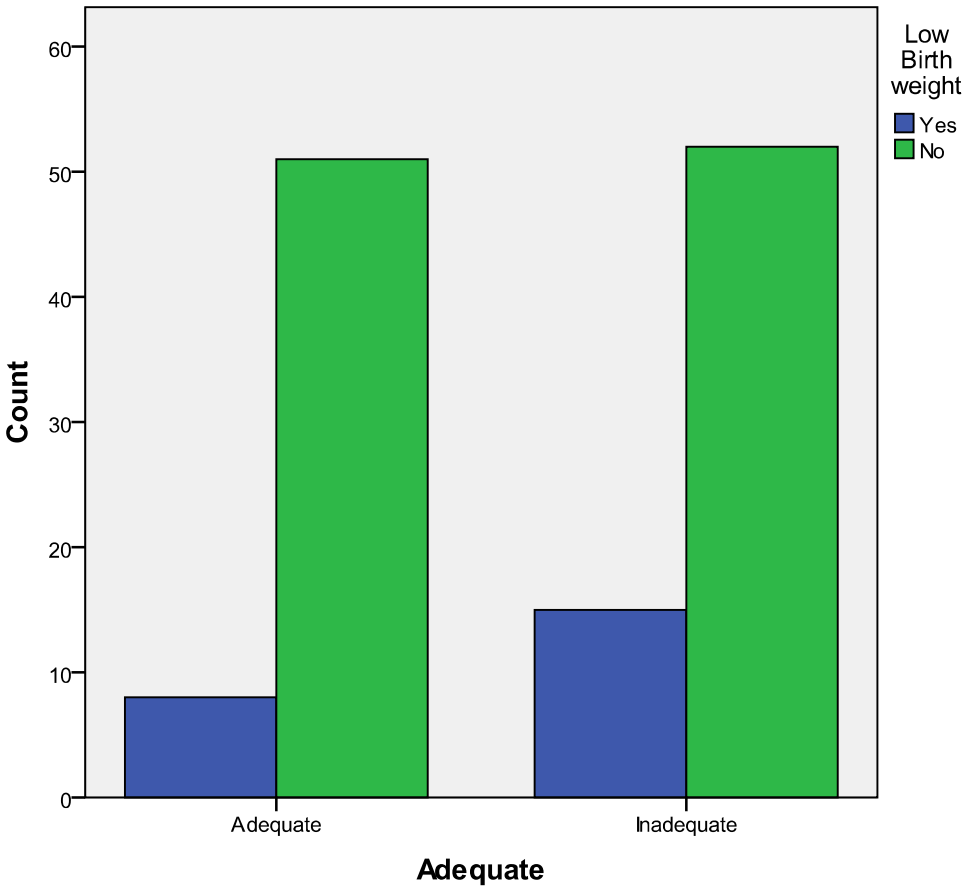
Chi square value 1.639

Df= 1

Sig value= 0.147

P value= >0.01

This table shows that 13.6% of our patients in the adequately treated group delivered low birth weight babies while 22.4% of patients in the inadequately treated group delivered low birth weight babies.


Low Birth weight
Yes
No
Count
60
50
40
30
20
10
0
Adequate
Inadequate
Adequate

DISCUSSION

This study was conducted in PSG Institute of Medical Sciences and Research during the period of March 2011 to August 2012.

The purpose of the study was to follow the pregnancy outcomes in pregnant women with hypothyroidism to see whether they developed complications if left untreated and if adequate treatment altered the occurrence of complications.

The total number of pregnant women included in this study were 126.All women with diagnosed hypothyroidism and started on treatment delivering over a period of 1 1//2 yrs were taken consecutively.

All antenatal women were screened using TSH at their first booking visit. Those who had an elevated TSH levels, were further tested with FT4 and started on treatment with levothyroxine irrespective of whether FT4 was elevated or not. The cut-off level for TSH was taken as 3mIU/ml. Serum thyrotropin (TSH) level in early pregnancy is decreased because of thyroid stimulation from the weak TSH effects of HCG. In a study by Green WL in 2005, truly normal range of TSH is defined as 0.5-2.5mIU/ml(6). So adequate replacement therapy should be given when TSH is above 3mIU/ml and/or with low T4, FT4 in pregnancy.

Patients with TSH values between 3-5mIU/ml were started on a dose of 25microgram and those with levels from 5-10mIU/ml were given 50microgram.Those with levels above 10mIU/ml were started on higher doses after

consulting with the endocrinologist. It was not possible for all patients with an elevated TSH to undergo further testing with FT4 for many reasons like some being already started on treatment if they had already been diagnosed preconceptionally or if they had been started on treatment even before FT4 levels were available. So, a classification of these patients into a subclinical hypothyroid group and overt hypothyroid group was not possible.

TSH levels were repeated for these patients 4-6 weeks after initiating the treatment or atleast in each trimester and thyroxine dosage titrated accordingly. Based on whether they were started on treatment before 10 weeks and given prompt dosage titration, they were grouped as those receiving adequate treatment and inadequate treatment. A patient was considered to have received adequate treatment if the repeat TSH values were less than 3 mIU/ml Both the groups were followed till delivery and closely observed for the development of complications.

Out of the 126 patients studied, 59 patients were adequately treated,while 67 patients received inadequate treatment. Out of the 59 adequately treated patients only 7 developed complications(11.9%).But 43 out of the 67 patients receiving inadequate treatment developed complications(64.2%).

Thyroid hormone is essential for normal development of the placenta. There is evidence that preeclampsia, placental abruption and preterm labour are causally

linked to faulty early placentation. Hypothyroid mothers are also at an increased risk of developing fetal growth restriction and delivering low birth weight babies.(12)

The results of our study revealed that gestational diabetes.GDM was found in 12 out of the 126 hypothyroid patients(9.5%).Overt diabetes was also found in 2 patients. showing a possible relationship between hypothyroidism and glucose intolerance9quote incidence in gen popln).

Approximately 12-15% of clinically recognised pregnancies, end in spontaneous miscarriage (24). In our study the prevalence of blighted ovum was 1.5% and missed abortion was 4.5%and 3% had incomplete abortion in the inadequately treated group in our study. Put together the overall miscarriage rate was 9% which is actually lower than that of its expected occurrence. It was also noted that in our study group , the women who had miscarriages had higher TSH values at diagnosis(>5mU/L).

Preeclampsia is identified in 3.9% of all pregnancies (48) .The prevalence of pregnancy induced hypertension (gestational hypertension and preeclampsia) was 14.9% in the group which was inadequately treated in our study. Davis et al 1988 followed 25 hypothyroid women through 28 pregnancies who were divided into two groups, of which 16 were clinically hypothyroid and 12 had subclinical hypothyroidism. This study showed that mothers with overt hypothyroidism are more at risk for preeclampsia.

Inadequately treated hypothyroid women in our study had 9% pregnancies complicated by Oligohydramnios which was higher than its expected occurrence in late pregnancies(3.9%) in the general population.

In our study population 20.9% of pregnancies ended up in preterm delivery (delivery before 37 weeks of gestation) which was similar to the outcome of a study done by Jones WS et al in the American Journal of Obstetrics and Gynaecology in 1969 who concluded that premature deliveries were more frequent in pregnant women who had low thyroxine levels.

In our study 7.4% of the foetuses of inadequately treated mothers had intrauterine growth restriction which was almost similar to its occurrence in the general population.(3-10%)

Out of the 67 inadequately treated patients in our study, 15 women delivered babies with low birth weight (22.4%), whereas, only 8 women in the adequately treated group had low birth weight babies (13.6%). But, Low birth weight among these babies was mainly attributed to prematurity.

There was no case of placental abruption in the inadequately treated patients in my study although Casey Brian et al in 2005 in their study concluded that pregnancies complicated by subclinical hypothyroidism had a 3 fold increased risk of

developing placental abruption and 2 fold increased risk of preterm labour compared to euthyroid women .

CONCLUSION

Thyroid hormone is essential for early placental development in pregnancy. Especially during the first twelve weeks of pregnancy the fetus entirely depends upon the the maternal thyroid hormone for the normal neural and skeletal development. Hence early diagnosis and adequate treatment of maternal hypothyroidism in pregnancy is essential in decreasing the incidence of complications like abortion, pre eclampsia, IUGR, placental abruption, oligohydramnios and low birth weight which are associated with hypothyroidism.

Inadequately treated hypothyroid women in my study group had a 3 fold increased risk of developing preeclampsia.

There was no significant increase in the incidence of abortion or fetal growth restriction in the inadequately treated group.

The incidence of GDM in my study is 10.5%

There was no case of placental abruption in my study group.

Oligohydramnios was found to occur more commonly in the inadequately treated group.

Adequate treatment significantly reduced certain complications like pre eclampsia,

PROFORMA

Name:

Age:

OP.NO:

IP.NO:

Obstetric score:

H/O Infertility:Yes/No

Gestational Age at diagnosis:

Gestational Age at which treatment was started:

Drug &Dosage used:

	At diagnosis	After treatment
TSH		
fT4		

Previous pregnancy:

(any significant past H/O)

Present Pregnancy:

(any antenatal complications)

Gestational age at delivery:

Mode of delivery:

Baby details:

Birth weight-

APGAR-

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CONSENT FORM

I, Mrs._____ aged _____ years have been adequately well explained in the language that I understand regarding the clinical screening and blood investigations that are to be carried out with me. The purpose of the study was explained to me prior to this study being done in detail. I understood that the confidentiality will be maintained regarding identity. I have been well explained and willing to undergo oral thyroxine supplementation therapy.

After understanding the basis of this study, I give my full consent to the study.

Name of the patient:
Signature of the patient:
Date and Time:

Name of the investigator:
Signature:

KEY TO MASTER CHART

OBSTRETIC SCORE

1. PRIMI PARA
2. MULTI PARA

GESTATIONAL AGE AT DIAGNOSIS

1. PRECONCEPTIONAL
2. LESS TAHN 10 WEEKS
3. MORE THAN 10 WEEKS

TSH AT DIAGNOSIS

1. 3-5 mIU / ml
2. 5-10 mIU / ml
3. MORE THAN 10 mIU / ml

ADEQUACY OF TREATMENT

1. ADEQUATE
2. INADEQUATE

GESTATIONAL AGE AT DELIVERY

1.LESS THAN 37 WEEKS

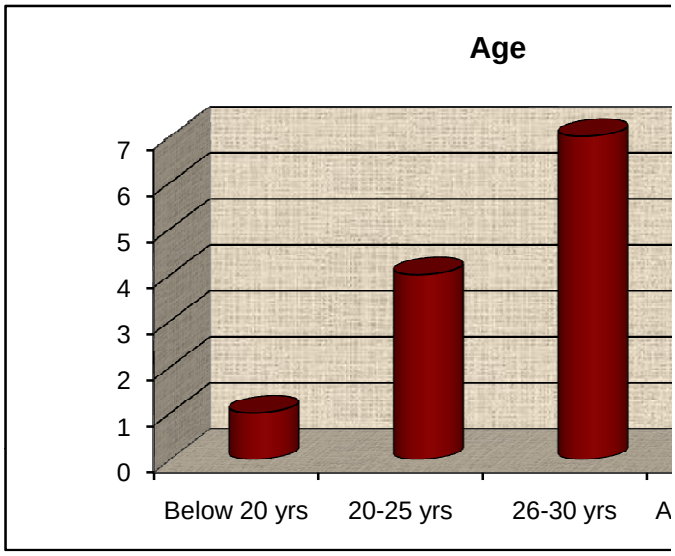
2.MORE THAN 37 WEEKS

BIRTH WEIGHT

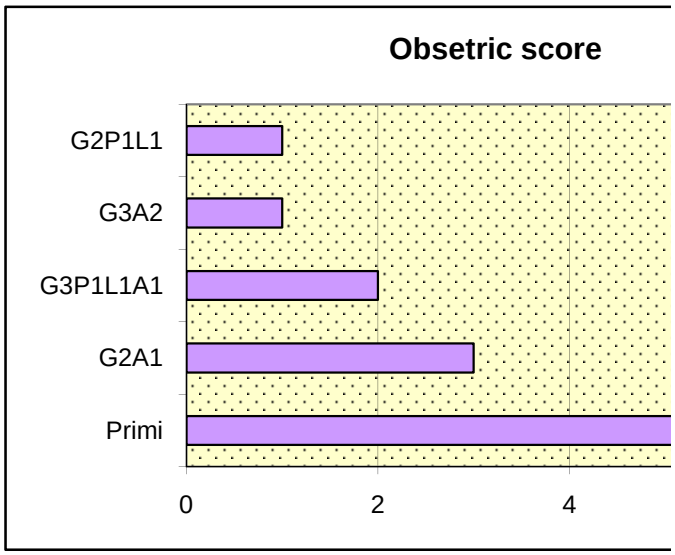
1.LESS THAN 2.5Kgs

2.MORE THAN 2.5Kgs

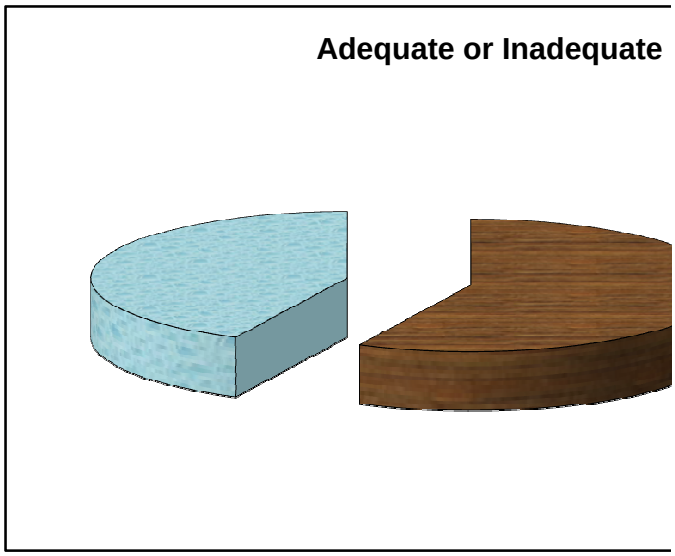
Age	No of respondents	Percentage
Below 20 yrs	1	7.14
20-25 yrs	4	28.57
26-30 yrs	7	50
Above 30 yrs	2	14.28
Total	14	100

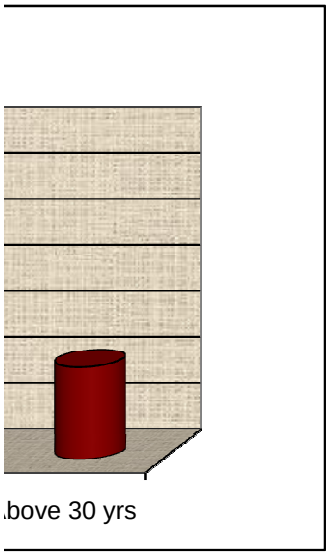


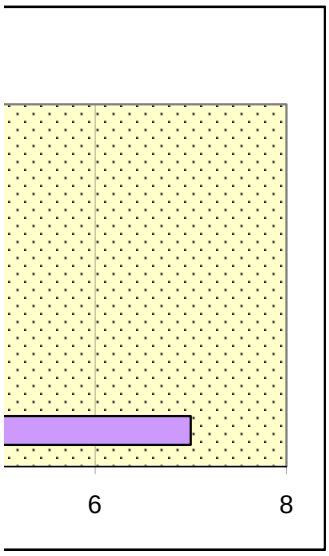
Obs Score	No of respondents	Percentage
Primi	7	50
G2A1	3	21.42
G3P1L1A1	2	14.28
G3A2	1	7.14
G2P1L1	1	7.14
Total	14	100

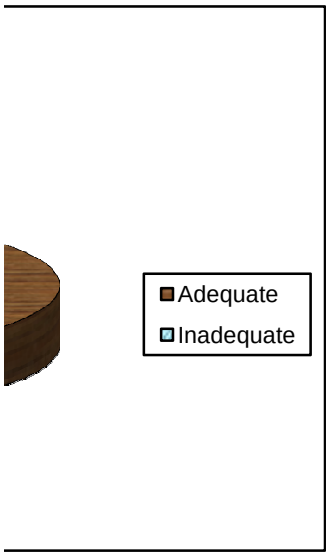


Adequate or Inadequate	No of respondents	Percentage
Adequate	8	57.14
Inadequate	6	42.86
Total	14	100




bove 30 yrs


6
8


Adequate
Inadequate

v	Name	OP Number	Age	Obsscore	Gest age at diagn	TSH	FT4	Rx
1	Vaishnavi		22	2	1	2	1.04	Thyroxine 25 mg
2	Selvinandhu		29	1	3	2	10.8	Thyroxine 25mg
3	Revathy		28	1	3	3		Thyroxine 100mg
4	Epseba		28	1	2	2		No Rx
5	Subbulakshmi		35	1	1	2		Thyroxine 25mg
6	Dhanalakshmi		25	2	2	2		Thyroxine 25 mg
7	Hemapriya		19	1	1	2		No Rx
8	madhavi		23	2	3	2		Thyroxine 50 mg
9	Ambika		27	1	3	3	1.9	Thyroxine 100mg
10	Indhu		32	2	3	2		Thyroxine 50 mg
11	Subashini		26	2	2	2		Thyroxine 50 mg
12	Christy bai		30	2	2	3		Thyroxine 50 to 125 mg
13	Arthee Ragunathan		30	1	3	2		Thyroxine 50 mg
14	Saranya		25	2	2	2		Thyroxine 25 mg
15	Nithya devi	O11033610	28	2	1	2		Thyroxine 50 mg
16	Pandeeshwari	O09094688	24	1	3	1		Thyroxine 100 mg
17	Deepa	O11060899	29	2	1	3		No Rx
18	Latha	O10102270	38	1	3	3	0.62	Thyroxine 100 mg
19	Yamuna	O11094850	32	2	1	3		Thyroxine 100 mg
20	Thenmozhi	O10069730	28	2	2	3	1.3	Thyroxine 50 mg
21	Sasikala	O11008964	24	1	1	2		Thyroxine 12.5 mg
22	Rajeswari	O07020200	25	2	2	2		Thyroxine 25mg
23	Amutha bharathi	O07033914	33	2	1	2		No Rx
24	Suji kumari	O11030574	38	1	2	2		Thyroxine 25mg
25	Thulasi mani	O10058981	34	2	3	2		No Rx
26	Anitha	O11001543	26	1	1	2		Thyroxine 12.5 mg
27	Vasavi	O11013245	28	2	2	2	0.9	Thyroxine 25mg
28	Janani	O11024853	26	1	1	2		No Rx
29	Renukadeepa	O11051733	28	1	1	3		Thyroxine 50 mg
30	Usha nandhini	O11043550	30	2	2	2	2.16	Thyroxine 100mg
31	Kalaiselvi	O10107140	29	1	3	2		Thyroxine 50 mg
32	Anitha	O11063379	25	1	2	3		Thyroxine 100 mg
33	Akilandam	O09068082	25	2	3	2		Thyroxine 100 mg
34	Dr. Vasanthi	O05032611	37	2	3	3		Thyroxine 100 mg
35	suganthi	O11087136	28	1	1	2		Thyroxine 50 mg
36	ramya	O12002464	27	2	2	1		Thyroxine 12.5 mg
37	hadlin vinothini	O11039561	28	1	1	1	0.92	Thyroxine 100 mg
38	jayamani	O08002895	33	2	1	2		No
39	kalpana	O10038695	27	1	2	1	0.9	Thyroxine 25 mg
40	rani	O11042200	29	2	3	1		Thyroxine 50 mg
41	gokila	O11048831	25	2	2	1	1.07	Thyroxine 25 mg
42	priskilal	O11051692	26	1	3	2	1.1	Thyroxine 25 mg
43	nagalakhmi	O09007892	26	2	3	2	0.9	Thyroxine 50 mg
44	banumathi	O11005533	28	1	1	2		no
45	sridevi	O11058613	24	2	2	2	0.94	Thyroxine 50 mg
46	shobana	I11005719	28	1	2	2		no
47	nandhini	O11083592	19	1	1	2	0.95	Thyroxine 75 mg
48	bharathi devi	O11044560	25	2	1	2		Thyroxine 25 mg
49	karthika	O12003418	24	1	2	2	1	Thyroxine 25 mg
50	roslin	O11049542	39	1	2	2		Thyroxin
51	ramila	O11097025	29	2	1	3		no
52	gowri	O11070363	21	1	1	2		Thyroxine 25 mg
53	sasirekha	O07042238	31	2	2	2	1.2	Thyroxine 50 mg
54	nandhini	O11047851	18	1	1	3	1.19	Thyroxine 25 mg
55	jamuna	O11056277	19	1	1	2	0.9	Thyroxine 25 mg
56	sathyavani	O11076207	34	1	2	2		Thyroxine 150 mg
57	Selvi	O11083866	33	1	3	2	0.8	no
58	gowri	O11057039	29	2	1	2		Thyroxine 100 mg
59	vinotha	O12006657	21	2	2	3	1.2	Thyroxine 150 mg
60	adhilakshmi	O11064036	22	2	3	3		Thyroxine 25 mg
61	antony tersa	O11083290	30	1	2	2	0.96	Thyroxine 100 mg
62	kavitha	O11069776	23	2	2	3	0.91	Thyroxine 25 mg
63	nithya	O11062816	23	1	1	2		no
64	vidya	O11070400	22	1	1	2	1.12	Thyroxine 25 mg
65	priya	O11041832	23	2	2	2		Thyroxine 25 mg
66	kalpana	O11044496	29	2	1	2		Thyroxine 50 mg
67	manju jancy	O11022028	27	1	3	2		Thyroxine 25 mg
68	Dhanalakshmi	O06046895	32	2	3	2		Thyroxine 75 mg
69	meena	O08018408	27	2	3	3		Thyroxine 25 mg
70	leema	O11055688	32	2	3	3		Thyroxine 100 mg
71	sudha	O07041575	28	1	2	2		Thyroxine 50 mg
72	anitha	O08015422	26	2	3	3		Thyroxine 100 mg
73	shyni	O11075075	30	2	2	2	2.3	Thyroxine 50 mg
74	jennathul	O0804588	22	2	1	2		Thyroxine 50 mg
75	rabiya	O08039005	27	2	3	2		Thyroxine 250 mg
76	vijayalakshmi	O11079382	28	1	3	2		Thyroxine 50 mg
77	ambika devi	O11083770	35	1	3	2		Thyroxine 100 mg
78	kavithamani	O11026822	25	2	3	2		Thyroxine 75 mg
79	shalini	O11046688	27	1	2	2		Thyroxine 25 mg
80	vanitha	O11036955	26	2	1	2		Thyroxine 25 mg
81	dharani	O09069139	25	2	1	3		Thyroxine 50 mg
82	deepa	O11035331	21	1	2	2	1.02	Thyroxine 100 mg
83	shobana	O11050897	19	1	1	2		Thyroxine 25 mg

84	geetha	O11032180	28	2	3	1	1.06	Thyroxine 50 mg
85	ananthi	O08037124	30	2	3	2		Thyroxine 50 mg
86	lavanya	O11030700	21	1	2	2		Thyroxine 50 mg
87	saraswathi	O10057417	26	2	1	2		Thyroxine 50 mg
88	ameena	O11062159	28	2	2	2		Thyroxine 25 mg
89	sarmila	O11093663	30	2	3	2		no
90	mahalakshmi	O11041761	32	2	2	2		Thyroxine 25 mg
91	Uma Maheshwari	O12041431	26	1	1	1		Thyroxine 25 mg
92	Thangalakshmi	O12051864	27	1	1	2		Thyroxine 25 mg
93	Kayalvizhi	O11085962	26	2	1	2		Thyroxine 25mg
94	Angeline	O11088064	26	1	1	2		Thyroxine 25 mg
95	Umadevi	O12024847	23	1	2	2		no
96	Manimegalai	O11094144	32	1	1	2		Thyroxine 25mg
97	Catherine jona	O11090367	27	2	3	2		Thyroxine 150mg
98	Ramathilagam	O11078403	26	2	1	2		Thyroxine 25mg
99	Tamilselvi	O11082251	29	2	3	2		Thyroxine 25mg
100	Sanjitha	O11012370	26	2	1	2		Thyroxine 25mg
101	Srividya	O12032626	23	1	3	2		Thyroxine 75mg
102	Manjula	O12003484	31	2	2	2		Thyroxine 75mg
103	Jothi	O12040865	29	2	3	2		Thyroxine 75mg
104	Maleswari	O11031696	22	1	1	2		Thyroxine 25mg
105	Nithyadevi	O12014102	21	1	2	2		Thyroxine 100mg
106	Jenifer	O12000192	23	1	2	3		Thyroxine 50mg
107	Thangamani	O09103105	22	2	3	2		Thyroxine 100mg
108	Nilofer	O12042981	25	1	2	2		Thyroxine 100mg
109	Priya	O07049300	22	1	1	2		Thyroxine 25mg
110	Kavitha	O12045806	27	1	2	3		no
111	Subashini	O09045097	26	1	2	2		Thyroxine 25mg
112	Sumathi	O07083900	34	2	1	2		Thyroxine 100mg
113	sathyapriya	O08090325	24	2	2	2		Thyroxine 25mg
114	Jeevitha	O11059073	25	2	2	2		Thyroxine 100mg
115	Arasi	O11075271	26	1	2	2		Thyroxine 25mg
116	Sathyabala	O08027280	29	2	1	2		Thyroxine 100mg
117	Sukumari laxman	O10095890	33	1	1	2		Thyroxine 25mg
118	Vimala	O12029430	33	1	3	2		Thyroxine 25mg
119	Priya	O09071039	31	2	2	2		Thyroxine 25mg
120	Kavitha	O09070205	27	2	2	2		Thyroxine 50 mg
121	Hemalatha	O11081015	21	1	1	2		Thyroxine 100mg
122	Baby	O10062614	34	2	3	2		Thyroxine 50mg
123	Abirami	O11082925	24	1	2	2		no
124	Selvi	O11071578	21	1	1	2		Thyroxine 25mg
125	Sofia	O12035614	26	1	2	2		Thyroxine 25mg
126	Anitha rajan	O08046404	25	1	1	2		Thyroxine 25mg

Rpt TSH	Ade/Inade	Complication	Other comorbidities	Mode of delivery	GA at del	Birth weight
3.63	1	No	Nil	Emergency LSCS	2	2
	1	No	Nil	NVD	2	2
3.2	1	No	Nil	Emergency LSCS	2	2
	2	IUGR Absent diast flow	Nil	Emergency LSCS	2	2
	1	No	GDM on diet	Vacuum	2	1
3.36	2	No	Encerclage	NVD	2	2
	2	IUGR Absent diast flow		NVD	2	2
3.5	1	No	Nil	NVD	2	2
0.23	1	No	Rh negative	NVD	2	2
3.7	1	No	Nil	Emergency LSCS	2	2
1.6	2	PPROM	GDM on diet	Preterm delivery	1	1
2.34	2	No		NVD	2	2
2.8	1	No		Emergency LSCS	2	2
	2	Severe Preeclampsia		Preterm delivery	1	1
2.7	1	No	nil	Emergency LSCS	2	1
	2	PIH		NVD	2	2
	2	Missed abortion				
3.1	2	PROM	nil	Emergency LSCS	2	2
	2			Emergency LSCS	2	2
2.3	2	Severe Preeclampsia	nil	Emergency LSCS	2	2
9.5	2	No	GDM on diet	Emergency LSCS	2	2
4	2	No	no	Vacuum	2	2
	2	Incomplete abortion				
0.4	2	Oligohydramnios	Rh negative	Emergency LSCS	2	2
	2	Missed abortion				
	1	No		NVD	2	1
6.9	2	No		Emergency LSCS	2	2
	2	Incomplete abortion				
	1	No		NVD	2	2
0.56	2	PROM		Emergency LSCS	2	2
	1	No		NVD	2	2
5.2	2	IUGR Absent dicst flow		Emergency LSCS	2	2
0.27	1	No		Elective LSCS	2	2
2.2	1	No		Elective LSCS	2	1
1.2	2			Preterm delivery	1	1
	1	No		NVD	2	2
1.34	1	No		NVD	2	2
6	2	No		Vacuum	2	2
2.2	1	No		NVD	2	2
	1	No	Nil	Elective LSCS	2	2
3.14	1	PROM	Anemia corrected	NVD	2	2
2.3	2	PPROM		Preterm delivery	1	1
9.2	2	Blighted ovum	Rh negative			
	2	PROM		Emergency LSCS	2	2
	2	No	TPO +ve	Emergency LSCS	2	2
	2	Missed abortion				
3.2	1	No		NVD	2	2
2.6	1	No		NVD	2	2
	2	No		Vacuum	2	2
	2	PIH, impaired GCT		Emergency LSCS	2	2
	1	No	Anemia corrected	Emergency LSCS	2	2
	2	No	no	Elective LSCS	2	2
	2	PIH	seizure disorder	Elective LSCS	2	2
2.5	1	No		NVD	2	1
2.2	1	PROM		NVD	2	2
3.2	2	Oligohydramnios		Emergency LSCS	2	2
	2	Oligohydramnios		Emergency LSCS	2	2
	2	No		Elective LSCS	2	2
	2	No	GDM on insulin pre.LSCS	NVD	2	2
2.6	1	No		Emergency LSCS	2	2
	2	Impaired GCT		NVD	2	2
9	1	PROM	Prev LSCS	Emergency LSCS	2	2
	1	No		Emergency LSCS	2	2
3.2	2	No	GDM on diet	Emergency LSCS	2	2
	2	PROM	NO	Vacuum	2	2
6.3	1	Chronic	GDM on insulin	Emergency LSCS	2	2
	1	No	GDM on diet	NVD	2	2
2.9	2	No		Preterm delivery	1	1
13.6	1	No		NVD	2	2
	2	No	GDM on diet	NVD	2	2
4.1	1	2nd trimester abortion				
	1	No		NVD	2	2
	2	No		Elective LSCS	2	2
3.98	1	Severe Preeclampsia		NVD	2	1
	2	Oligohydramnios		Preterm delivery	1	1
4.2	1	Oligohydramnios	Overt DM	Preterm delivery	1	1
	2	No		NVD	2	2
2.6	1	Oligohydramnios		Vacuum	2	2
	2	No		NVD	2	2
1.35	1	No		Vacuum	2	2
	1	No		NVD	2	2
	2	No		Vacuum	2	2
	1	No	chronic HW Rh	NVD	2	2

1.95	1	No		Preterm delivery	1	1
2.56	1	No	no	NVD	2	2
3.5	2	PPROM	no	Preterm delivery	1	1
3.9	2	No		Elective LSCS	2	2
5.3	2	PIH	GDM on diet	Vacuum	2	1
	2	PROM	GDM on insulin	Vacuum	2	2
3.3	2	No	GDM on insulin	Preterm delivery	1	1
	1	No		NVD	2	2
	1	No		NVD	2	2
	1	No		NVD	2	2
	1	No		Vacuum	2	2
	2	No		NVD	2	1
	1	No		Vacuum	2	2
	1	No		Vacuum	2	2
	1	No		Elective LSCS	2	2
	2	PPROM		Preterm delivery	1	1
	2	No		Preterm delivery	1	1
	1	No		Elective LSCS	2	2
	2	oligohydramnios		Emergency LSCS	2	2
	1	No		Elective LSCS	2	2
	1	No		Emergency LSCS	2	2
	2	No		Emergency LSCS	2	2
	2	No		Vacuum	2	2
	2			Preterm delivery	1	1
	2	PPROM	Chronic HTN	Preterm delivery	1	1
	1	No		Emergency LSCS	2	2
	2	Severe Preeclampsia		Emergency LSCS	2	2
	2	PIH		Emergency LSCS	2	2
	1	No		NVD	2	2
	2	No		NVD	2	2
	2	PIH		NVD	2	2
	2	No		NVD	2	2
	1	No		Elective LSCS	2	2
	1	No	Rh -ve Cervical fibroid	Elective LSCS	2	2
	1	No	Overt DM,short stature	Elective LSCS	2	2
	2	oligohydramnios		NVD	2	2
	2	IUGR		Elective LSCS	2	2
	1	No	GDM on insulin	Forceps delivery	2	2
	1	No		NVD	2	2
	2			NVD	2	2
	1	No		NVD	2	2
	2	PPROM		Preterm delivery	1	1
	1	No	Rh -ve	Emergency LSCS	2	2